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=> fil capl; d que l14; d que l16; d que l26; d que l31; s l14 or l16 or l26 or l31
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FILE LAST UPDATED: 13 Jan 2002  (20020113/ED)

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L6          9219 SEA FILE=CAPLUS ABB=ON  ALLOGEN?
L7           112 SEA FILE=CAPLUS ABB=ON  ALLOACTIVAT?
L8           733 SEA FILE=CAPLUS ABB=ON  ANTIGENICALLY DISTINCT
L9        133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L10          742 SEA FILE=CAPLUS ABB=ON  L9(L)((L6 OR L7 OR L8))
L11        25426 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L13          516 SEA FILE=CAPLUS ABB=ON  L9(L)L11
L14            4 SEA FILE=CAPLUS ABB=ON  L13 AND L10


L6          9219 SEA FILE=CAPLUS ABB=ON  ALLOGEN?
L7           112 SEA FILE=CAPLUS ABB=ON  ALLOACTIVAT?
L8           733 SEA FILE=CAPLUS ABB=ON  ANTIGENICALLY DISTINCT
L9        133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L10          742 SEA FILE=CAPLUS ABB=ON  L9(L)((L6 OR L7 OR L8))
L15         5041 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CT OR THERAP?(L)IMMUNO/OB
                 I
L16           10 SEA FILE=CAPLUS ABB=ON  L10 AND L15
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L9        133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L11        25426 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L15         5041 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CT OR THERAP?(L)IMMUNO/OB
                 I
L17         1046 SEA FILE=CAPLUS ABB=ON  L9(L)(MIX##### OR COCULTUR? OR CO
                 CULTUR?)
L26            2 SEA FILE=CAPLUS ABB=ON  L17 AND L11 AND L15


L6          9219 SEA FILE=CAPLUS ABB=ON  ALLOGEN?
L7           112 SEA FILE=CAPLUS ABB=ON  ALLOACTIVAT?
L8           733 SEA FILE=CAPLUS ABB=ON  ANTIGENICALLY DISTINCT
L9        133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L10          742 SEA FILE=CAPLUS ABB=ON  L9(L)((L6 OR L7 OR L8))
L11        25426 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L15         5041 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CT OR THERAP?(L)IMMUNO/OB
                 I
L17         1046 SEA FILE=CAPLUS ABB=ON  L9(L)(MIX##### OR COCULTUR? OR CO
                 CULTUR?)
L27       167362 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#
L28        28436 SEA FILE=CAPLUS ABB=ON  L27(3A)(ACTIVAT? OR L7 OR STIMULAT?)
L31            5 SEA FILE=CAPLUS ABB=ON  (L11 OR L15) AND L28 AND (L10 OR L17)


L161          18 L14 OR L16 OR L26 OR L31

=> fil cancer; d que l61; fil wpids; d que l89; fil embase; d que l135; d que l144; s
l135 or l144
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 FILE COVERS 1963 TO 14 Jun 2001 (20010614/ED)

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L46        14703 SEA FILE=CANCERLIT ABB=ON  ALLOGEN?
L47          128 SEA FILE=CANCERLIT ABB=ON  ALLOACTIVAT?
L48          291 SEA FILE=CANCERLIT ABB=ON  ANTIGENICALLY DISTINCT
L49        18444 SEA FILE=CANCERLIT ABB=ON  LYMPHOCYTES/CT
L52        22876 SEA FILE=CANCERLIT ABB=ON  IMMUNOTHERAPY+NT/CT
L56          201 SEA FILE=CANCERLIT ABB=ON  L49(L)TR/CT
L57         6932 SEA FILE=CANCERLIT ABB=ON  L49(L)IM/CT
L59         9253 SEA FILE=CANCERLIT ABB=ON  L49/MAJ
L60          377 SEA FILE=CANCERLIT ABB=ON  L59 AND (L46 OR L47 OR L48)
L61           10 SEA FILE=CANCERLIT ABB=ON  L60 AND L56 AND L57 AND L52


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TR = transplantation
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L77	588	SEA FILE=WPIDS ABB=ON	ALLOGEN?
L78	6	SEA FILE=WPIDS ABB=ON	ALLOACTIVAT?
L79	5711	SEA FILE=WPIDS ABB=ON	LYMPHOCYTE# OR LYMPHO CYTE#
L80	11	SEA FILE=WPIDS ABB=ON	ANTIGENICALLY DISTINCT?
L81	1132	SEA FILE=WPIDS ABB=ON	IMMUNOTHERAP? OR IMMUNO THERAP?
L82	14050	SEA FILE=WPIDS ABB=ON	VACCINE# OR VACCINAT?
L84	853	SEA FILE=WPIDS ABB=ON	L79(5A)(ACTIVAT? OR STIMULAT?)
L88	14	SEA FILE=WPIDS ABB=ON	(L77 OR L80)(5A)L84 OR L78
L89	3	SEA FILE=WPIDS ABB=ON	L88 AND (L81 OR L82)

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FILE COVERS 1974 TO 10 Jan 2002 (20020110/ED)

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L125	36705	SEA FILE=EMBASE ABB=ON	LYMPHOCYTE/CT
L126	229	SEA FILE=EMBASE ABB=ON	ALLOACTIVAT?
L127	25501	SEA FILE=EMBASE ABB=ON	ALLOGEN?
L128	762	SEA FILE=EMBASE ABB=ON	ANTIGENICALLY DISTINCT
L131	42929	SEA FILE=EMBASE ABB=ON	IMMUNOTHERAPY+NT/CT
L132	13938	SEA FILE=EMBASE ABB=ON	VACCINE/CT OR TUMOR VACCINE/CT OR TUMOR CELL VACCINE/CT OR CANCER VACCINE/CT
L135	1	SEA FILE=EMBASE ABB=ON	(L126 OR L127 OR L128) AND L125 AND L131 AND L132

L125	36705	SEA FILE=EMBASE ABB=ON	LYMPHOCYTE/CT
L126	229	SEA FILE=EMBASE ABB=ON	ALLOACTIVAT?
L127	25501	SEA FILE=EMBASE ABB=ON	ALLOGEN?
L128	762	SEA FILE=EMBASE ABB=ON	ANTIGENICALLY DISTINCT
L131	42929	SEA FILE=EMBASE ABB=ON	IMMUNOTHERAPY+NT/CT
L132	13938	SEA FILE=EMBASE ABB=ON	VACCINE/CT OR TUMOR VACCINE/CT OR TUMOR CELL VACCINE/CT OR CANCER VACCINE/CT
L136	24960	SEA FILE=EMBASE ABB=ON	L125/MAJ
L137	23830	SEA FILE=EMBASE ABB=ON	L131/MAJ
L138	10669	SEA FILE=EMBASE ABB=ON	L132/MAJ
L139	2960	SEA FILE=EMBASE ABB=ON	LYMPHOCYTE#(5A)(ACTIVAT? OR STIMULAT?) AND (L127 OR L128)
L141	8991	SEA FILE=EMBASE ABB=ON	LYMPHOCYTE ACTIVATION/CT
L143	256348	SEA FILE=EMBASE ABB=ON	"BLOOD AND HEMOPOIETIC SYSTEM"/CT
L144	11	SEA FILE=EMBASE ABB=ON	(L139 OR L126 OR L141) AND L136 AND (L137 OR L138) AND L143

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L162          12 L135 OR L144

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L150     234206 SEA FILE=BIOSIS ABB=ON  LYMPHOCYTE#
L151        210 SEA FILE=BIOSIS ABB=ON  ALLOACTIVAT?
L152      28996 SEA FILE=BIOSIS ABB=ON  ALLOGEN? OR ANTIGENICALLY DISTINCT
L153        794 SEA FILE=BIOSIS ABB=ON  L150(5A)L152(5A)(ACTIVAT? OR STIMULAT?)

L154         84 SEA FILE=BIOSIS ABB=ON  L150(5A)L151
L155      85371 SEA FILE=BIOSIS ABB=ON  VACCINE# OR VACCINAT?
L156      28855 SEA FILE=BIOSIS ABB=ON  IMMUNOTHERAP? OR IMMUNO THERAP?
L160          6 SEA FILE=BIOSIS ABB=ON  (L153 OR L154)(15A)(L155 OR L156)


=> dup rem l61,l161,l160,l162,l89
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PROCESSING COMPLETED FOR L160
PROCESSING COMPLETED FOR L162
PROCESSING COMPLETED FOR L89
L163          49 DUP REM L61 L161 L160 L162 L89 (0 DUPLICATES REMOVED)
                 ANSWERS '1-10' FROM FILE CANCERLIT
                 ANSWERS '11-28' FROM FILE CAPLUS
                 ANSWERS '29-34' FROM FILE BIOSIS
                 ANSWERS '35-46' FROM FILE EMBASE
                 ANSWERS '47-49' FROM FILE WPIDS

=> d ibib ab 1-49

L163 ANSWER 1 OF 49  CANCERLIT
ACCESSION NUMBER:    93283237  CANCERLIT
DOCUMENT NUMBER:     93283237
```

TITLE: Cellular interaction against autologous tumor cells between IL-2-cultured lymphocytes and fresh peripheral blood lymphocytes in patients with breast cancer given immuno-chemotherapy.
AUTHOR: Yamasaki S; Kan N; Mise K; Harada T; Ichinose Y; Moriguchi Y; Kodama H; Satoh K; Ohgaki K; Tobe T
CORPORATE SOURCE: First Department of Surgery, Faculty of Medicine, Kyoto University, Japan.
SOURCE: BIOTHERAPY, (1993). Vol. 6, No. 1, pp. 63-71.
Journal code: AU3. ISSN: 0921-299X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 93283237
ENTRY MONTH: 199308
AB In patients with Stage II or III breast cancer and in patients with liver metastases from breast cancer, we examined cellular interaction in the cytotoxicity against autologous tumor cells by interleukin-2(IL-2)-cultured lymphocytes (CL) and fresh peripheral blood lymphocytes (FPBL) treated with immunochemotherapy including OK-432 and cyclophosphamide. In flow cytometric analysis, CD8+CD11b+ and CD16+ cells significantly decreased after immuno-chemotherapy in both groups of patients. A protocol study in Stage II or III breast cancer patients showed suppressive activity of FPBL on the cytotoxic activity of CL in 3/9 of the non-treatment group but no suppressive activity and enhancing activity in 3/7 in the immuno-chemotherapy group. Moreover, in 19 patients with liver metastases from breast cancer treated with immuno-chemotherapy including adoptive immunotherapy, FPBL in 6/19 showed enhancing activity, and in 8/19 suppressive activity in the lysis of autologous tumor cells. In assays in vitro using autologous and **allogeneic** tumor cells, FPBL showed a partial specificity in cellular interaction against autologous tumor cells. CD4-depleted FPBL inhibited cytotoxicity of CL, while CD8-depleted FPBL enhanced cytotoxicity of CL in patients with liver metastases. These results suggest that immuno-chemotherapy eliminates the suppressive population in FPBL and may induce tumor regression if combined with adoptive immunotherapy using CL.

L163 ANSWER 2 OF 49 CANCERLIT
ACCESSION NUMBER: 90141977 CANCERLIT
DOCUMENT NUMBER: 90141977
TITLE: The effects of perioperative portal venous inoculation with donor lymphocytes on renal allograft survival in the rat. I. Specific prolongation of donor grafts and suppressor factor in the serum.
AUTHOR: Yoshimura N; Matsui S; Hamashima T; Lee C J; Ohsaka Y; Oka T
CORPORATE SOURCE: Second Department of Surgery, Kyoto Prefectural University of Medicine, Japan.
SOURCE: TRANSPLANTATION, (1990). Vol. 49, No. 1, pp. 167-71.
Journal code: WEJ. ISSN: 0041-1337.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 90141977
ENTRY MONTH: 199004
AB In order to investigate the in vivo functional role of the liver in the immune responses in organ transplantation, effects of perioperative portal venous p.v. administration of donor lymphocytes on renal allograft survival were tested in the rat kidney transplant model. Donor lymphocytes were prepared from BN (BN, RT-1n) or third-party DA (RT1a) rat spleens and lymph nodes and injected p.v. or intravenously to Lewis (LEW, RT-1l) hosts on the day of transplantation (day 0). Untreated LEW hosts rejected BN renal grafts at 7.8 +/- 0.6 days (n = 10). Intravenous administration of 1

x 10(8) BN cells to LEW hosts on day 0 caused a slight, but not significant, prolongation of renal allograft survival (MST = 9.5 +/- 3.0 days, n = 13, NS), whereas portal venous inoculation of 1 x 10(8) BN cells on day 0 remarkably prolonged renal graft survival to 22.2 +/- 5.3 (n = 10, P less than 0.01). The prolongation of graft survival was antigen-specific; the administration of 1 x 10(8) DA cells p.v. to LEW hosts did not prolong the survival of BN renal grafts (MST = 7.4 +/- 0.8, n = 5). Spleen cells from p.v. treated LEW hosts 10 days after transplantation had no suppressor effect on the one-way MLC reaction of normal LEW responder cells toward donor BN or third-party DA stimulators. On the other hand, when serum from p.v.-treated LEW hosts was added to MLC at a concentration of 3 per cent of total volume, it suppressed the MLC reaction toward donor BN cells by 71.6 per cent, but not toward third-party DA stimulators (-8.5 per cent suppression, NS). Histological examination of p.v.-treated LEW hosts at 10 days after transplantation revealed that the liver had normal lobular architecture without expansion of portal tracts and infiltration of inflammatory cells. On the other hand, the transplanted kidney demonstrated a moderate mononuclear cell infiltration around the artery without an interstitial hemorrhage. Moreover, adoptive transfer of the serum from p.v.-treated LEW rats into the virgin secondary LEW hosts significantly prolonged the graft survival of BN kidneys from 7.8 days to 18.9 +/- 5.5 days (P less than 0.01), but not third-party DA graft survivals (MST = 7.5 +/- 0.6 days), indicating that an antigen-specific tolerogenic factor was released into the circulation through the process of **allogeneic** cells in the liver.

L163 ANSWER 3 OF 49 CANCERLIT
ACCESSION NUMBER: 90090450 CANCERLIT
DOCUMENT NUMBER: 90090450
TITLE: Therapeutic efficacy of human recombinant interleukin-2 (TGP-3) alone or in combination with cyclophosphamide and immunocompetent cells in **allogeneic**, semi-syngeneic, and syngeneic murine tumors.
AUTHOR: Ootsu K; Gotoh K; Houkan T
CORPORATE SOURCE: Central Research Division, Takeda Chemical Industries Ltd, Osaka, Japan.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1989). Vol. 30, No. 2, pp. 71-80.
Journal code: CN3. ISSN: 0340-7004.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 90090450
ENTRY MONTH: 199003
AB The potential for a recombinant human interleukin-2 (rIL-2, TGP-3) alone, in combination with cyclophosphamide, and in combination with cyclophosphamide and normal immunocompetent cells to manifest biological activity in vivo was tested using **allogeneic**, semi-syngeneic, and syngeneic tumor-host systems in mice. The biological activity of rIL-2 was evaluated by the inhibition of the growth of tumors and the inhibition of metastases in short-term assays and, in long-term assays, the prolongation of the survival time of mice bearing subcutaneously (s.c.) or intradermally transplanted tumors. rIL-2 was injected s.c. daily continuously for up to 40 days or intermittently two to four times into mice bearing established tumors. In the short-term assays, the dose and schedule dependence of activity of rIL-2 alone was significantly manifested against sarcoma 180 in ICR mice (**allogeneic**) by the regression of the tumor, and was confirmed against Meth-A fibrosarcoma in BALB/c mice (syngeneic) by retarding the growth of the tumor. When assessed using these tumor, it was found that the antitumor activity of rIL-2 was schedule-dependent: the growth of tumors was more significantly suppressed when rIL-2 was injected every day for 10 days, starting on the

7th day after tumor transplantation, than when rIL-2 was injected five times every other day or twice every 5th day, even if the total amounts of rIL-2 injected were same. The continuous injection for 10 days was considered to be a standard regimen and the daily effective doses of rIL-2 were 5, 10, and 25 micrograms/mouse. Using the standard regimen and the effective doses, the activity of rIL-2 alone was also observed against two other syngeneic tumors: Colon carcinoma 26 in BALB/c mice, by retarding the growth of the tumor, and Lewis lung carcinoma in C57BL/6 mice by reducing the formation of lung metastases. When assessed using M5076 reticulum cell sarcoma, in a long-term assay, the activity of rIL-2 alone was not manifested in C57BL/6 mice (syngeneic) even when rIL-2 was injected for a long period (20 days) but it was observed in BDF1 (semi-syngeneic) mice. On the other hand, it was found that rIL-2 was effective in combination with cyclophosphamide in prolonging the survival time of C57BL/6 mice bearing the tumor.(ABSTRACT TRUNCATED AT 400 WORDS)

L163 ANSWER 4 OF 49 CANCERLIT
ACCESSION NUMBER: 88150876 CANCERLIT
DOCUMENT NUMBER: 88150876
TITLE: Clinical adoptive chemoimmunotherapy with **allogeneic alloactivated** HLA-haploidentical lymphocytes: controlled induction of graft-versus-host-reactions.
AUTHOR: Kohler P C; Hank J A; Minkoff D Z; Sondel P M
CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin, Madison.
CONTRACT NUMBER: CA 32685 (NCI)
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1988). Vol. 26, No. 1, pp. 74-82.
Journal code: CN3. ISSN: 0340-7004.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 88150876
ENTRY MONTH: 198805
AB A total of 13 cancer patients were treated with Adoptive Chemoimmunotherapy (ACIT) using **alloactivated** HLA haploidentical lymphocytes. Donor lymphocytes were activated in vitro using a pool of irradiated **allogeneic** lymphocytes (MLC-cells) and some further expanded by culturing in T-cell growth factor (TCGF-cells). The first 6 patients received i.v. cyclophosphamide (CPM) followed 24 h later by escalating doses of MLC-cells, then 7 days later they received an infusion of TCGF-cells. Minimal toxicity was seen. The next 7 patients received CPM (800 mg/m2) and a combined MLC and TCGF-cell infusion (total cell dose ranged from 0.79 x 10(10) to 2.26 x 10(10)). Of these 7 patients, 3 developed mild graft-versus-host reaction (GVHR) which resolved without treatment, and 2 patients had progressive GVHR which was arrested by methylprednisolone (2 mg/kg). Peripheral blood lymphocytes from these 2 patients, during the GVHR, had increased activated T-cells (OKT-10+ and OK-Ia+). In vitro expansion, in TCGF, of these activated T-cells enabled HLA typing to prove they were of donor origin. Only 1 clinical antitumor response was observed in the first 6 patients. The results of this study indicate that this form of ACIT can be given to patients with acceptable toxicity. Self-limited or easily controlled GVHR may be induced and primed donor cells persisting in the circulation are probably responsible. Further testing is required to determine whether the immune response induced by this form of ACIT may be therapeutically effective.

L163 ANSWER 5 OF 49 CANCERLIT
ACCESSION NUMBER: 86009665 CANCERLIT
DOCUMENT NUMBER: 86009665
TITLE: Alloantigen-activated lymphocytes from mice bearing a spontaneous "nonimmunogenic" adenocarcinoma inhibit its

growth in vivo by recruiting host immunoreactivity.
AUTHOR: Giovarelli M; Santoni A; Forni G
SOURCE: JOURNAL OF IMMUNOLOGY, (1985). Vol. 135, No. 5, pp. 3596-603.
Journal code: IFB. ISSN: 0022-1767.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Abridged Index Medicus Journals; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 86009665
ENTRY MONTH: 198512
AB Nylon wool columns eluting lymphocytes from the spleen of mice bearing a clinically evident spontaneous, nonimmunogenic adenocarcinoma of recent origin (TS/A) do not display cytotoxic response, release of lymphokines, and proliferation in vitro against TS/A cells, nor do they inhibit TS/A tumor growth in a Winn-type neutralization assay in vivo. After 5-day co-culture with **allogeneic** spleen cells from mice differing at multiple minor histocompatibility antigens only, these lymphocytes are still noncytolytic against TS/A cells, whereas they release interferon-gamma, mediate delayed-type hypersensitivity (DTH) reactions, and inhibit TS/A tumor growth in the Winn assay. In the Winn test, **alloactivated** lymphocytes from TS/A tumor-bearing mice are more effective than those from normal mice on a per cell basis. The induction of this TS/A tumor inhibition ability depends on the presence in the cultures of Thy-1+ lymphocytes. The presence of Lyt-2+ lymphocytes is also important, whereas that of asialo GM1+ is not. The TS/A inhibition in vivo by **alloactivated** lymphocytes mostly depends on Thy-1+, Lyt-2- and asialo GM- lymphocytes, even though a few Thy- cells are also very efficient tumor inhibitors. The **alloactivated** lymphocytes inhibit TS/A tumor growth by recruiting the radiosensitive effector mechanisms of the recipient mice required for ultimate tumor rejection. TS/A tumor rejection leaves a specific DTH and an immunologic memory resulting in rejection of a second lethal TS/A challenge in a significant number of mice.

L163 ANSWER 6 OF 49 CANCERLIT
ACCESSION NUMBER: 85074044 CANCERLIT
DOCUMENT NUMBER: 85074044
TITLE: Clinical response of a patient with diffuse histiocytic lymphoma to adoptive chemoimmunotherapy using cyclophosphamide and **alloactivated** haploidentical lymphocytes. A case report and phase I trial.
AUTHOR: Kohler P C; Hank J A; Exten R; Minkoff D Z; Wilson D G; Sondel P M
CONTRACT NUMBER: CA-32685 (NCI)
GM 07131 (NIGMS)
SOURCE: CANCER, (1985). Vol. 55, No. 3, pp. 552-60.
Journal code: CLZ. ISSN: 0008-543X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Abridged Index Medicus Journals; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 85074044
ENTRY MONTH: 198503
AB Adoptive chemoimmunotherapy has cured experimentally induced tumors in animals, but its clinical use has been limited. Six patients were treated with refractory neoplasms in a Phase I study with cyclophosphamide (CPM) and **alloactivated** haploidentical lymphocytes. Patients received an immunosuppressive dose of CPM (800 mg/m2) followed by haploidentical lymphocytes primed in vitro with alloantigens in mixed lymphocyte culture (MLC). One week later patients received a second infusion of **alloactivated** lymphocytes expanded in T-cell growth factor (TCGF). The total number of cells given to each patient progressively increased,

with a single patient receiving 35.5 X 10(9) cells. Transient febrile responses and delayed-type hypersensitivity reactions at the intravenous sites were the only toxicities noted. A complete clinical response lasting 12 weeks was seen in a single patient with diffuse histiocytic lymphoma. Our experience indicates that adoptive chemoimmunotherapy can be given to patients safely and merits further clinical testing.

L163 ANSWER 7 OF 49 CANCERLIT
ACCESSION NUMBER: 85057050 CANCERLIT
DOCUMENT NUMBER: 85057050
TITLE: Intralesional injection of interleukin-2-expanded autologous lymphocytes in melanoma and breast cancer patients: a pilot study.
AUTHOR: Adler A; Stein J A; Kedar E; Naor D; Weiss D W
SOURCE: JOURNAL OF BIOLOGICAL RESPONSE MODIFIERS, (1984). Vol. 3, No. 5, pp. 491-500.
Journal code: JBM. ISSN: 0732-6580.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 85057050
ENTRY MONTH: 198502
AB The clinical effect of intralesional injection of interleukin-2 (IL-2)-cultured autologous lymphocytes was assessed in seven patients with cutaneous, recurrent tumor nodules (12 melanoma and 8 mammary cancer lesions). Each tumor nodule was injected 3-10 times, once weekly, with IL-2-cultured lymphoid cells (CLC), 40-400 million cells at each injection. Lymphoid cells obtained from buffy coats were separated on Ficoll-Paque, cryopreserved in liquid nitrogen, thawed, and cultured for 1-2 weeks in the presence of crude IL-2 (containing phytohemagglutinin) before injection. CLC were tested for sterility, percent E-rosette-forming cells, and cytotoxicity against K562, **allogeneic** melanoma, and breast cancer cell lines and autologous tumor cells. Enhanced cytotoxicity was expressed by IL-2 CLC, as compared with nonstimulated peripheral blood lymphocytes (PBL). Arrest of tumor growth (compared with untreated lesions) was observed in eight lesions and partial regression in three lesions. Moreover, complete regression was noted in one large melanoma lesion treated with low-dose irradiation prior to intralesional administration of CLC and in three small intracutaneous melanoma lesions treated with CLC only. Histopathological findings of responding lesions showed infiltration with lymphoid cells and macrophages, with the tumor cells sparsely dispersed. No untoward side effects of CLC injections were observed. The present study points to the feasibility of trials of adoptive immunotherapy in cancer patients as indicated by the following: (a) response of lymphoid cells to IL-2 adequate--although reduced--in patients with metastatic disease, including those after chemo- or radiotherapy; (b) possibility of cryopreservation of PBL and repeated culturing in IL-2 after thawing, with cytotoxic activity unimpaired; (c) demonstrably enhanced cytotoxicity in vitro of IL-2 CLC; (d) demonstrable--although limited--clinical response to in situ treatments with IL-2 CLC; (e) good tolerance of treatment with CLC.

L163 ANSWER 8 OF 49 CANCERLIT
ACCESSION NUMBER: 85110602 CANCERLIT
DOCUMENT NUMBER: 85110602
TITLE: Rationale for a novel immunotherapy of cancer with **allogeneic** lymphocyte infusion.
AUTHOR: Kondo M; McCarty M F
SOURCE: MEDICAL HYPOTHESES, (1984). Vol. 15, No. 3, pp. 241-77.
Journal code: M0M. ISSN: 0306-9877.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
FILE SEGMENT: MEDL; L; Priority Journals

LANGUAGE: English
OTHER SOURCE: MEDLINE 85110602
ENTRY MONTH: 198504
AB A simple method of cancer immunotherapy has been developed which achieves marked objective response in 20-30% of patients with disseminated disease. Each course consists of a low dose of chemotherapy followed two days later by intravenous infusion of **allogeneic** lymphocytes. Courses are repeated on a monthly basis as needed. The function of the chemotherapy--too mild to significantly influence tumor growth directly--appears to be depletion of suppressor T cells, which sensitizes the patient to the immunostimulant action ("**allogeneic** effect") of the subsequently infused lymphocytes. The rationale for this method is discussed in the context of a review of past attempts at lymphocyte immunotherapy. We are now attempting to improve response rates by combatting anergy with nutritional immunopotentiators, and by preventing prostaglandin-mediated or -dependent immunosuppression with prostaglandin synthetase inhibition. By understanding and counteracting the various specific and general means by which a growing tumor induces host tolerance, it should prove possible to achieve immune-mediated tumor regression in a high proportion of patients. Best results may be seen when **allogeneic** lymphocyte therapy is initiated at an earlier stage of the disease, and is used in conjunction with surgery, radiotherapy, short-course intensive chemotherapy, or hyperthermia-based methods.

L163 ANSWER 9 OF 49 CANCERLIT
ACCESSION NUMBER: 84173463 CANCERLIT
DOCUMENT NUMBER: 84173463
TITLE: Inhibition of human melanoma growth in nude mice by autologous, **alloactivated** peripheral blood lymphocytes.
AUTHOR: Balsari A; Fossati G; Taramelli D; Nava M; Ravagnani F; Parmiani G
SOURCE: TUMORI, (1984). Vol. 70, No. 1, pp. 35-9.
Journal code: WJS. ISSN: 0300-8916.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 84173463
ENTRY MONTH: 198406
AB Peripheral blood lymphocytes of melanoma patients were stimulated in vitro by a pool of **allogeneic** lymphocytes and shown to be cytotoxic against autologous melanoma cells. To evaluate the in vivo antitumor activity of the cytotoxic **alloactivated** autologous peripheral blood lymphocytes, tumor neutralization (Winn) assay was carried out by injecting such lymphocytes admixed with autologous melanoma cells in athymic BALB/c nude mice. In 3 of 6 cases, complete inhibition of tumor growth was obtained at lymphocytes to tumor cells ratio of 10:1 and in one case also of 5:1. In all cases the appearance of tumors was delayed and the growth rate was significantly reduced in a dose-dependent fashion as compared to control mice injected with tumor cells alone. We conclude that in vitro **alloactivated** peripheral blood lymphocytes can inhibit and/or impair the growth of autologous melanoma cells in nude mice.

L163 ANSWER 10 OF 49 CANCERLIT
ACCESSION NUMBER: 83258936 CANCERLIT
DOCUMENT NUMBER: 83258936
TITLE: The role of **allogeneic** cells in the stimulation of cell-mediated cytotoxicity to leukaemia cells. A family study.
AUTHOR: Taylor G M; Bradley B A
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1983). Vol. 15, No. 1, pp. 39-46.
Journal code: CN3. ISSN: 0340-7004.

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 83258936
ENTRY MONTH: 198310

AB **Allogeneic** lymphocytes can stimulate cell-mediated cytotoxicity (CMC) in lymphocytes from leukaemia patients against autologous leukaemia target cells. We have compared the capacity of different **allogeneic** lymphoid cells to stimulate CMC to fresh (i.e., patient) and cultured (MOLT 4, K562) leukaemic target cells in lymphocytes from an acute leukaemic patient and his HLA-identical siblings. **Allogeneic** lymphoid cells, and particularly a lymphoblastoid cell line, were effective in stimulating CMC to leukaemia targets. In some instances, however, leukaemia cells derived from the patient, mixed with **allogeneic** lymphoid cells stimulated synergistic CMC to the patient's leukaemia. We also found that the patient's leukaemia cells alone were able to stimulate CMC in HLA-identical sib lymphocytes to fresh and cultured leukaemia targets. Extra specificities on fresh leukaemia cells were revealed when these cells induced unpredicted CMC on normal lymphocyte targets when added to mixed lymphocyte cultures (MLC) between related and unrelated lymphocytes. Cytotoxic lymphocytes generated in MLC against the patient's HLA antigens were absorbed by monolayers of lymphocytes and leukaemia cells of the same HLA type as the patient, leaving residual CMC to fresh (patient) and cultured (K562) leukaemia target cells. In addition, CMC to the patient's leukaemia cells, stimulated in lymphocytes from the patient's HLA-identical sib by **allogeneic** cells, was absorbed by a monolayer of these **allogeneic** cells. This suggests cross reactivity between determinants on the leukaemia and **allogeneic** lymphocytes. The results of this study are consistent with expression of 'leukaemia antigen', which are not restricted to leukaemia cells but may also be expressed on lymphocytes.

L163 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:636194 CAPLUS
DOCUMENT NUMBER: 135:194468
TITLE: Hybrid cell vaccines derived by fusion of an allogeneic dendritic cells and a non-dendritic cells and uses in tumor and infection therapy
INVENTOR(S): Kanz, Lothar; Walden, Peter; Stuhler, Gernot
PATENT ASSIGNEE(S): Eberhard-Karls-Universitaet Tuebingen Universitaetsklinikum, Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062902	A1	20010830	WO 2000-EP2433	20000320
W: AE, AG, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MA, MD, MG, MN, MW, MX, NO, NZ, PL, RU, SD, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10009030	A1	20010920	DE 2000-10009030	20000227
EP 1130088	A1	20010905	EP 2000-105829	20000320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DE 2000-10009030 A 20000227
US 2000-185334 P 20000228

AB The present invention relates to methods and compns. for treating and preventing cancer and infectious disease using hybrid cells formed by fusion of allogeneic dendritic cells and autologous non-dendritic cells which shares at least one class I MHC (major histocompatibility complex) allele. Such hybrid cells combine the vigorous alloreactivity of mature dendritic cells with the specific antigenicity of autologous tumor cells, thereby eliciting a highly specific and vigorous cytotoxic T lymphocytes (CTL) response. The invention also provides the methods for making hybrid cell vaccines and evaluating its cytotoxicity. For rapid and large-scale generation of hybrids, electrofusion is established as a two-step procedure: in the first step, tumor cells and dendritic cells (DCs) were dielectrophoretically aligned to from cell-cell conjugates; in the second step, a fusion pulse was applied, yielding 10-15% hybrid cell formation. The invention demonstrates that vaccine with tumor cell-dendritic cell hybrid results in regression of human metastatic renal cell carcinoma.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:695169 CAPLUS
DOCUMENT NUMBER: 135:370366
TITLE: Crystal structures of two closely related but antigenically distinct HLA-A2/melanocyte-melanoma tumor-antigen peptide complexes
AUTHOR(S): Sliz, Piotr; Michielin, Olivier; Cerottini, Jean-Charles; Luescher, Immanuel; Romero, Pedro; Karplus, Martin; Wiley, Don C.
CORPORATE SOURCE: Department of Molecular and Cellular Biology and Howard Hughes Medical Institute, Harvard University, Cambridge, MA, 02138, USA
SOURCE: J. Immunol. (2001), 167(6), 3276-3284
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have detd. high-resoln. crystal structures of the complexes of HLA-A2 mols. with two modified immunodominant peptides from the melanoma tumor-assocd. protein Melan-A/Melanoma Ag recognized by T cells-1. The two peptides, a decamer and nonamer with overlapping sequences (ELAGIGILTV and ALGIGILTV), are modified in the second residue to increase their affinity for HLA-A2. The modified decamer is more immunogenic than the natural peptide and a candidate for peptide-based melanoma immunotherapy. The crystal structures at 1.8 and 2.15 .ANG. resoln. define the differences in binding modes of the modified peptides, including different clusters of water mols. that appear to stabilize the peptide-HLA interaction. The structures suggest both how the wild-type peptides would bind and how three categories of cytotoxic T lymphocytes with differing fine specificity might recognize the two peptides.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:671411 CAPLUS
DOCUMENT NUMBER: 134:221307
TITLE: Semi-**allogeneic** cell hybrids stimulate HIV-1 envelope-specific cytotoxic T **lymphocytes**
AUTHOR(S): Grene, Edith; Newton, Danforth A.; Brown, Edwin A.; Berzofsky, Jay A.; Gattoni-Celli, Sebastiano; Shearer, Gene M.
CORPORATE SOURCE: Experimental Immunology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: AIDS (London) (2000), 14(11), 1497-1506
CODEN: AIDSET; ISSN: 0269-9370
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was designed to det. whether the HLA allogeneic T helper response stimulated by semi-allogeneic cell lines could be used as an in vitro model of immune-based therapy to stimulate HIV-specific cytotoxic T lymphocytes. Semi-allogeneic cell hybrids were obtained by the fusion of peripheral blood mononuclear cells from HIV-infected patients with the allogeneic .beta.2-microglobulin-deficient FO1-12 melanoma cell line. These hybrids were used as antigen presenting cells for HIV envelope peptide (env)-specific cytotoxic assays. The hybrid cell lines express HLA class I and II antigens from both parental cells, as well as the CD86 costimulatory mol. HIV-specific cytotoxic T lymphocyte activity was obtained when patients" blood mononuclear cells were costimulated with env peptides plus semi-allogeneic hybrids, in contrast with stimulation with either env or hybrid cells alone. Thus, the semi-allogeneic hybrids enhanced HIV-specific killing of target cells. Irradiated, semi-allogeneic cell hybrids engineered for individual AIDS patients provide efficient and simultaneous co-recognition of HLA allogeneic determinants and viral antigenic determinants presented by self-HLA mols. on the same antigen presenting cells and results in the generation of enhanced HIV-specific cytotoxic T lymphocyte activity.
REFERENCE COUNT: 30
REFERENCE(S): (1) Abdel-Wahab, Z; Cell Immunol 1996, V171, P246 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:370632 CAPLUS
DOCUMENT NUMBER: 134:16336
TITLE: Antigen-specific cancer immunotherapy using a GM-CSF secreting allogeneic tumor cell-based vaccine
AUTHOR(S): Chang, Edwin Y.; Chen, Chien-Hung; Ji, Hongxiu; Wang, Tian-Li; Hung, Kenneth; Lee, Bruce P.; Huang, Alex Y. C.; Kurman, Robert J.; Pardoll, Drew M.; Wu, T.-C.
CORPORATE SOURCE: Department of Pathology, School of Medicine, The Johns Hopkins University, Baltimore, MD, USA
SOURCE: Int. J. Cancer (2000), 86(5), 725-730
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Granulocyte-macrophage colony-stimulating factor (GM-CSF)-transduced autologous tumor cell-based vaccines are currently one of the major forms of cancer vaccines. However, the prepn. of GM-CSF-transduced autologous tumor vaccines is time-consuming and tech. challenging. In addn., the host antigen presenting cells, rather than the tumor vaccine cells themselves, present tumor-specific antigens and prime the host T cells. Therefore, we tested the efficacy of antigen-specific allogeneic tumor vaccines. We used human papillomavirus 16 (HPV-16) E7 protein as a model tumor antigen, which is assocd. with the development of most cervical carcinoma. B16, a C57BL/6 (H-2b) derived melanoma cell line, was genetically engineered to produce GM-CSF alone (B16GM), HPV-16 E7 alone (B16E7), or both (B16GME7). These vaccine cells were injected into BALB/c (H-2d) mice (106 cells/mouse). Two weeks later, mice were challenged with 105 live HPV-16 E7+ BL-I (H-2d) tumor cells and monitored for tumor progression twice weekly. To det. the effective cell population in the antitumor immunity elicited by B16GME7, we carried out in vivo antibody depletion expts. using CD4 and CD8 specific antibodies. In addn., as a measure of the immune responses produced by B16GME7, we performed an in vitro cytotoxic T lymphocyte assay using a std. chromium release method. We found that all of the mice vaccinated with B16GME7 remained tumor free 49 days post-BL-I challenge. In contrast, mice vaccinated with B16GM and B16E7 did not show any tumor protection against a similar dose of BL-I cells. Furthermore, the antitumor immunity produced by B16GME7 was dependent on both CD4 and CD8 T cells. In addn., E7-specific cytotoxic T lymphocyte activity could be readily demonstrated in mice immunized with B16GME7. These results suggest that allogeneic tumor cells transduced with GM-CSF and the tumor antigen, HPV-16 E7, cannot only generate an E7-specific cytotoxic T lymphocytes response in vitro, but can also elicit a potent antitumor immune response against an E7 expressing tumor in vivo.
REFERENCE COUNT: 31
REFERENCE(S): (3) Dranoff, G; Proc nat Acad Sci (Wash) 1993, V90, P3539 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:228317 CAPLUS
DOCUMENT NUMBER: 133:16149
TITLE: Interleukin-2 gene-transduced human leukemic cells induce major histocompatibility complex-restricted and -unrestricted anti-leukemic effectors in **mixed lymphocyte**-tumor cultures
AUTHOR(S): Cignetti, Alessandro; Guarini, Anna; Gillio Tos, Anna; Reato, Gigliola; Foa, Robert
CORPORATE SOURCE: Dipartimento di Scienze Biomediche ed Oncologia Umana, University of Torino, Turin, Italy
SOURCE: Cancer Gene Ther. (2000), 7(2), 167-176
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Nature America, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To explore the feasibility of designing vaccination protocols in acute leukemia patients with cytokine gene-transduced leukemic cells, the authors studied in vitro the growth potential of human leukemic cells transduced with the interleukin-2 (IL-2), IL-7, or IL-7 plus IL-2 genes, as well as the capacity of generating both autologous and allogeneic cytotoxic lymphocytes directed against the parental cells. A

lymphoblastic T-cell line, ST4, obtained from a patient in long-lasting complete remission, was retrovirally engineered with the IL-2, IL-7, and IL-7 plus IL-2 genes; in addn., clones releasing different amts. of the cytokines were obtained by limiting diln. Mixed lymphocyte-tumor cultures (MLTCs) were set up with parental or transduced leukemic cells as stimulators and with autologous or allogeneic lymphocytes as responders. When nonirradiated ST4 parental cells or clones producing <50 IU/mL/106 cells/72 h of IL-2 were used as stimulators, leukemic overgrowth was obsd. in MLTCs within 16 days of culture. When clones producing >80 IU/mL/106 cells/72 h of IL-2 were used as stimulators, the proliferation of leukemic cells was blocked and the transduced leukemic cells were completely cleared from the cultures by day 16; repeated restimulations with IL-2-producing leukemic cells were required to sustain long-term lymphocyte survival. On the contrary, when IL-7- or IL-7-IL-2-producing cells were used as stimulators, only a delay in leukemic cell overgrowth was obsd., and lymphocytes were completely cleared from the cultures after day 60. IL-7 prodn. by the different clones ranged between 11 and 36 ng/mL/106 cells/72 h, whereas the highest IL-2-producing IL-7-IL-2 clone released 50 IU/mL/106 cells/72 h of IL-2. When the stimulator efficacy of the highest IL-2-producing clone (ST4/IL-2#A7) was compared with that of exogenous IL-2 plus parental cells, a 7-fold higher amt. of exogenous IL-2 was required to achieve the same results obtained with IL-2-producing leukemic cells. Autologous and allogeneic long-term MLTCs (up to 35 days) with ST4/IL-2#A7 as the stimulator were capable of generating cytotoxic effectors equally endowed with both major histocompatibility complex (MHC) class I-unrestricted and -restricted activity against parental ST4 cells. By day 18 of both autologous and allogeneic cultures, a substantial proportion of CD56+ cells was consistently recorded; this was coupled to a predominantly MHC-unrestricted cytotoxic activity directed against parental ST4 cells. CD56+ cells decreased considerably at the end of the different MLTCs, together with the unrestricted cytotoxic activity. At this time, >50% of the cells were CD8+, and 55% of the activity could be blocked by an anti-MHC class I monoclonal antibody. Thus, IL-2 gene-transduced human acute leukemia cells cocultured with both autologous and allogeneic lymphocytes are capable of inducing a strong MHC-unrestricted anti-leukemic activity and subsequently "educating" MHC class I-restricted anti-leukemic effectors. The evidence that the immunogenic potential of human leukemic blasts can be boosted after transfer of the IL-2 gene suggests that the possibility of using leukemic cells engineered to release IL-2 as a therapeutic vaccine needs to be explored further.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:31906 CAPLUS
DOCUMENT NUMBER: 135:136184
TITLE: Correlation between enhancement of graft-versus-leukemia effects following **allogeneic** bone marrow transplantation by rIL-2 and increased frequency of cytotoxic T-**lymphocyte** precursors in murine myeloid leukemia
AUTHOR(S): Leshem, Benny; Vourka-Karussis, Urania; Slavin, Shimon
CORPORATE SOURCE: Lautenberg Center for General and Tumor Immunology,

Hebrew University-Hadassah Medical School, Jerusalem, Israel
SOURCE: Cytokines, Cell. Mol. Ther. (2000), 6(3), 141-147
CODEN: CCMTFO; ISSN: 1368-4736
PUBLISHER: Martin Dunitz Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A model of mouse acute myeloid leukemia (mAML) was used to study the effector mechanism mediating the graft-vs.-leukemia (GVL) effects in recipients of allogeneic bone marrow cells (BMC). MAML-bearing SJL/J (H-2s) mice were lethally irradiated and then transplanted with a mixt. of BMC and spleen cells (SC) derived from normal syngeneic or allogeneic mice. To augment the GVL effect, recipients were injected i.p. with recombinant human interleukin-2 (rIL-2) (1.2.times.105 IU) for 3 consecutive days, starting one day post BMC + SC transplantation. Spleen cells from treated recipients were adoptively transferred to untreated secondary SJL/J mice to test for the existence of residual tumor cells. All the secondary recipients of SC from mAML-bearing SJL/J mice rescued with syngeneic (SJL/J) or allogeneic (B10.S) BMC+SC (H-2s) differing at minor antigens of the histocompatibility complex (MiHC) developed leukemia and died. In sharp contrast, none of the secondary recipients of SC obtained from identical mAML-bearing mice rescued with B10.S BMC + SC but activated in vivo with IL-2 developed leukemia. Adoptive recipients of SC obtained from mAML-bearing recipients of major histocompatibility complex (MHC)-disparate (C57BL/6, H-2b) cells remained free of leukemia regardless of the use of rIL-2. In parallel with the in vivo findings, a 4-day in vitro exposure of splenocytes to 6.times.103 IU/mL rIL-2 resulted in a 5- to 20-fold increase in the frequency of alloreactive cytotoxic T-lymphocyte (CTL) precursors (CTLp) across MiHC and MHC barriers and a 2- to 6-fold increase in their cytotoxic activity. Our data suggest that augmentation of GVL effects by rIL-2 may be due to CTL activation by rIL-2, not excluding the potential beneficial role of rIL-2-activated allogeneic natural killer cells and MHC non-restricted killer cells. Cumulatively, our results suggest potentially beneficial effects of rIL-2, when used jointly with bone marrow transplantation or allogeneic cell therapy, on eradication of leukemia.
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:2111 CAPLUS
DOCUMENT NUMBER: 132:34451
TITLE: Vaccination of melanoma patients with interleukin 4 gene-transduced allogeneic melanoma cells
AUTHOR(S): Arienti, Flavio; Belli, Filiberto; Napolitano, Filomena; Sule-Suso, Josep; Mazzocchi, Arabella; Gallino, Gian Francesco; Cattelan, Alessandro; Sanantonio, Cristina; Rivoltini, Licia; Melani, Cecilia; Colombo, Mario Paolo; Cascinelli, Natale; Maio, Michele; Parmiani, Giorgio
CORPORATE SOURCE: Division of Experimental Oncology D, Instituto Nazionale per lo Studio e la Cura dei Tumori, Milan, 20133, Italy
SOURCE: Hum. Gene Ther. (1999), 10(18), 2907-2916
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A human melanoma line genetically modified to release interleukin 4 (IL-4) was utilized to immunize advanced melanoma patients in order to elicit or increase a specific anti-melanoma immune response, which may affect distant lesions. Twelve metastatic melanoma patients were injected s.c. at least three times with 5.times.107 IL-4 gene-transduced and irradiated allogeneic melanoma cells per dose. Both systemic and local toxicities were mild, consisting of transient fever and erythema, swelling, and induration at the vaccination site. Two mixed but not complete or partial clin. responses were recorded. To assess the immune response of vaccinated patients, both serol. and cell-mediated activities were evaluated. Antibodies to alloantigens could be detected in 2 of 11 patients tested. Mixed tumor-lymphocyte cultures were performed, utilizing autologous and allogeneic HLA-A2-matched melanoma lines as simulators and targets. A significant increase in IFN-.gamma. release was detected in 7 of 11 cases when postvaccination **lymphocytes** were **stimulated** by the untransduced allomelanoma cells. However, induction of a specific recognition of autologous melanoma cells by PBLs was obtained after vaccination in only one of six cases studied. This response involved the melanoma peptide Melan-A/MART-127-35 that was recognized in an HLA-A2-restricted fashion. These results indicate that vaccination with allogeneic melanoma cells releasing IL-4 locally can expand a T cell response against antigen(s) of autologous, untransduced tumor, although in a minority of patients.

REFERENCE COUNT: 45

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:673025 CAPLUS

DOCUMENT NUMBER: 134:221389

TITLE: Induction of preferential cytotoxicity against allogeneic mouse lymphoma cells: In vitro and in vivo studies

AUTHOR(S): Leshem, Benny; Dorfman, Yael; Kedar, Eli

CORPORATE SOURCE: The Lautenberg Center for General and Tumor Immunology, The Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel

SOURCE: Cancer Immunol. Immunother. (1999), 48(4), 179-188
CODEN: CIIMDN; ISSN: 0340-7004

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to activate, in mixed leukocyte/tumor cell cultures (MLTC), cytotoxic lymphocytes exhibiting preferential activity in vitro and in vivo towards allogeneic mouse lymphoma cells. Whereas the lymphoma target cells were readily lysed by the MLTC-derived lymphocytes, the cytotoxicity against the corresponding allogeneic concanavalin-A(ConA)-induced lymphoblasts was more than tenfold lower. Both activities were mediated by CD3+, TCR+, CD8+, CD4- cytotoxic T cells (CTL). ConA-induced lymphoblasts were readily lysed by anti-Thy 1.2 antibodies and complement, by CTL derived from mixed leukocyte cultures (MLC) and by the MLTC-derived CTL in the presence of ConA, indicating that the lymphoblasts are not merely less lysable than the lymphoma cells but that the latter are specifically recognized by the CTL. Lymphoblasts poorly competed with 51Cr-labeled lymphoma cells in a "cold"-target competition assay, suggesting that the MLTC-derived CTL largely recognize epitopes expressed only by the lymphoma cells. Furthermore, anal. of the cytotoxic activity of more than 500 MLTC-derived CTL oligoclones and over 30 clones revealed

that one-third of them were cytotoxic only against the allogeneic lymphoma cells, one-third were reactive against both the lymphoma and the allogeneic lymphoblast target cells and the remainder were not cytotoxic at all. Upon injection into sublethally irradiated, lymphoma-bearing allogeneic mice, the MLTC-derived CTL cured 56% of the recipients and caused graft vs. host disease (GVHD) is only 22%, whereas CTL activated in MLC against allogeneic splenocytes were therapeutically ineffective and caused lethal GVHD in 89% of the recipients. Although the therapeutic efficacy of the in vitro-generated antitumor CTL was demonstrated against exptl. lymphoma lines, this strategy might prove effective in tumor immunotherapy in conjuction with other modalities.

REFERENCE COUNT: 64
REFERENCE(S): (1) Alyea, E; Blood 1998, V91, P3671 CAPLUS
(6) Bergman, Y; Eur J Immunol 1977, V7, P413 CAPLUS
(7) Berke, G; Immunology 1983, V49, P585 CAPLUS
(12) Cerottini, J; Adv Immunol 1974, V18, P67 CAPLUS
(14) Charak, B; Blood 1992, V80, P179 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:543149 CAPLUS
DOCUMENT NUMBER: 129:172774
TITLE: Method for the production of selected lymphocytes
INVENTOR(S): Bell, David N.; Wong, Truman
PATENT ASSIGNEE(S): Hemosol Inc., Can.
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833891	A1	19980806	WO 1998-CA49	19980130
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9857447	A1	19980825	AU 1998-57447	19980130
AU 738538	B2	20010920		
EP 966523	A1	19991229	EP 1998-901286	19980130
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI				
US 6194207	B1	20010227	US 1998-16784	19980130

PRIORITY APPLN. INFO.: US 1997-37245 P 19970131
WO 1998-CA49 W 19980130

AB The invention is directed to methods for the prodn. of selected populations of lymphocytes. Lymphocytes produced can be isolated and purified using well known and established procedures to provide a consistent lymphocyte source which one of ordinary skill in the art can modify to provide an appropriate type or an optimal level of a desired lymphocyte. The availability of such cell populations allows not only for the complete reconstitution of the depleted, defective or missing lymphocyte population in a patient, but also provides the flexibility of having sufficient cells to permit multiple or cyclic treatments. These methods for expanding target cell populations are broadly applicable to the selective expansion of several types of lymphocytes and are demonstrated to maintain phenotype as well as antigen specificity.

L163 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:542991 CAPLUS
DOCUMENT NUMBER: 129:160641
TITLE: Cancer immunotherapy with semi-allogeneic cells
INVENTOR(S): Cohen, Edward P.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833527	A2	19980806	WO 1998-US1824	19980130
WO 9833527	A3	19981105		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1012240	A2	20000628	EP 1998-904782	19980130
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, IE				
US 6187307	B1	20010213	US 1998-16528	19980130
JP 2001522226	T2	20011113	JP 1998-533112	19980130

PRIORITY APPLN. INFO.: US 1997-36620 P 19970131
WO 1998-US1824 W 19980130

AB The present invention relates to improved semi-allogeneic immunogenic cells which act to stimulate and induce an immunol. response when administered to an individual. In particular, it relates to cells which express both allogeneic and syngeneic MHC determinants and which also express at least one antigen recognized by T lymphocytes. The invention is also directed to methods of inducing an immune response and methods of treating tumors by administering the semi-allogeneic immunogenic cells to an individual.

L163 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:251065 CAPLUS
DOCUMENT NUMBER: 128:307516
TITLE: Cancer immunotherapy using tumor cells combined with **mixed lymphocytes**
INVENTOR(S): Hiserodt, John C.; Thompson, James A.; Granger, Gale A.
PATENT ASSIGNEE(S): Regents of the University of California, USA; Hiserodt, John C.; Thompson, James A.; Granger, Gale A.
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816238	A2	19980423	WO 1997-US18718	19971010
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748242	A1	19980511	AU 1997-48242	19971010

CN 1237909	A	19991208	CN 1997-199908	19971010
BR 9712988	A	20001024	BR 1997-12988	19971010
US 6207147	B1	20010327	US 1997-948939	19971010
JP 2001509135	T2	20010710	JP 1998-517803	19971010
NO 9901691	A	19990609	NO 1999-1691	19990409

PRIORITY APPLN. INFO.: US 1996-28548 P 19961011
WO 1997-US18718 W 19971010

AB This invention comprises cellular vaccines and methods of using them in cancer immunotherapy, particularly in humans. The vaccines comprise **stimulated lymphocytes** allogeneic to the subject being treated, along with a source of tumor-assocd. antigen. The allogeneic **lymphocytes** can be **stimulated** by combining or coculturing them with leukocytes obtained from the subject to be treated or form another third-party donor. Tumor antigen may be provided in the form of primary tumor cells, tumor cell lines or tumor exts. prepd. from the subject. **Stimulated** allogeneic **lymphocytes** and tumor antigen are combined and administered at a site distant from the primary tumor, in order to prime or boost a systemic cellular anti-tumor immune response. This approach overcomes the natural refractory nature of the immune system to stimulation by tumor antigens, generating a host response and potentially improving the clin. outcome.

L163 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:207280 CAPLUS
DOCUMENT NUMBER: 133:236536
TITLE: Induction of antigen-specific T cells by allogeneic CD80 transfected human carcinoma cells
AUTHOR(S): Meyer, G. C.; Moebius, U.; Ruby, W.; Batrla, R.; Meuer, S. C.; Wallwiener, D.; Guckel, B.
CORPORATE SOURCE: Research Group Gene Therapy of Tumors, German Cancer Research Center, Heidelberg, 69120, Germany
SOURCE: Adv. Exp. Med. Biol. (1998), 451(Gene Therapy of Cancer), 195-202
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Expression of CD80 in breast carcinoma (MaCa) cells has been demonstrated to enable them to activate resting T cells in an HLA-matched situation and induce the generation of cytolytic T lymphocytes (CTLs). Since the same tumor cells were susceptible to the effector activity by in vitro preactivated CTL, the induction of the effector phase is not impaired. It was shown that the expression of adhesion mols. and MHC gene products on tumor cells was reduced as compared to professional antigen presenting cells (APCs). The study was also aimed at detg. at a quant. level and in comparison to professional APCs the ability of the allogeneic HLA-matched transfected MaCa variant KS-CD80 to induce antigen-specific T cells. The ability of this cell line to activate specific T cells in allogeneic situations was quantitated using a characterized viral T cell antigen MP57-68. It was obsd. that CD80 triggered an essential signal necessary for the expansion of antigen-specific T cells following antigen-presentation by KS-CD80 cells. Interferon-.gamma. and tumor necrosis factor-.alpha. treatment further augmented the response.

REFERENCE COUNT: 21
REFERENCE(S): (2) Boon, T; J Exp Med 1996, V183, P725 CAPLUS
(3) Chen, L; Cell 1992, V71, P1093 CAPLUS
(4) Disis, M; Cancer Res 1994, V54, P1071 CAPLUS
(10) Habicht, A; Eur J Cancer 1995, V31A, P2396 CAPLUS
(11) Lindauer, M; J Mol Med 1996, V74, P43 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:587361 CAPLUS

DOCUMENT NUMBER: 129:301664
TITLE: Granulocyte-macrophage colony-stimulating factor induces the differentiation of murine erythroleukemia cells into dendritic cells
AUTHOR(S): Cao, X.; Zhao, Y.; Yu, Y.; Wang, Y.; Zhang, M.; Zhang, W.; Wang, J.
CORPORATE SOURCE: Department of Immunology, Second Military Medical Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Immunology (1998), 95(1), 141-147
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dendritic cells (DC) are professional antigen-presenting cells (APC) within the immune system and antigen-pulsed DC can be used as an effective vaccine for active immunotherapy of cancer. Granulocyte-macrophage colony-stimulating factor (GM-CSF) plays an important role in the generation of DC. We previously showed that GM-CSF can induce murine erythroleukemia cells (FBL-3) to differentiate into monocyte-like cells. To develop a new vaccinating method to stimulate the host immune response to leukemia, we further investigate whether FBL-3 cells induced by GM-CSF can differentiate into DC in the present study. After being treated with GM-CSF, FBL-3 cells expressed high levels of 33D1 and NLDC-145, which are the specific markers of DC. The expression of MHC-II, B7-1, B7-2 and vascular cell adhesion mol.-1 (VCAM-1) was up-regulated markedly; the typical morphol. of DC were also obsd. by electron microscopy. Functionally, the GM-CSF-induced FBL-3 cells could apparently stimulate the proliferation of naive allogeneic and autologous T lymphocytes and induce the generation of specific CTL more efficiently than the wild-type FBL-3 cells. Mice immunized with GM-CSF-induced FBL-3 cells could resist the subsequent challenge with the wild-type FBL-3 cells. Collectively, these data indicate that GM-CSF differentiates murine erythroleukemia cells into DC phenotypically, morphol. and functionally. FBL-3-derived DC can be used as a new type of vaccine. Our results may have important implications for the immunotherapy of leukemia.

L163 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:269624 CAPLUS
DOCUMENT NUMBER: 126:329496
TITLE: Generation of primary tumor-specific cytotoxic T **lymphocytes** from autologous and human **lymphocyte** antigen class I-matched **allogeneic** peripheral blood **lymphocytes** by B7 gene-modified melanoma cells
AUTHOR(S): Yang, Sixun; Darrow, Timothy L.; Seigler, H. F.
CORPORATE SOURCE: Department of Surgery, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Cancer Res. (1997), 57(8), 1561-1568
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Expression of B7.1 costimulatory mols. on tumor cells has been shown to elicit antitumor immunity in mice. In the present study, we have developed a human B7.1 retroviral vector system to effectively transduce human melanoma cell lines and investigated the potential role of B7.1 in the generation of tumor-specific CTLs from peripheral blood lymphocytes (PBLs) in vitro. We have demonstrated that B7.1-modified melanoma cells are able to induce primary CTL activity from autologous, human lymphocyte antigen (HLA) class I-matched allogeneic PBLs and purified CD8+ T cells in the absence of exogenous cytokines. CTLs generated by B7.1 are tumor specific and HLA class I restricted, and CD8+ T cells are primarily responsible for this specific cytotoxicity. Furthermore, CTLs generated

from HLA class I-matched PBLs by B7.1 are cytolytic to tumor cells autologous to the stimulated PBLs. These data suggest that B7.1-modified tumor cells can be used as a potent tumor vaccine for both autologous and HLA class I-matched allogeneic patients.

L163 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:493552 CAPLUS
DOCUMENT NUMBER: 127:219277
TITLE: Increase of cytotoxic sensitivity of primary human melanoma cells transfected with the interleukin-7 gene to autologous and allogeneic immunologic effector cells
AUTHOR(S): Finke, Sigrun; Trojaneck, Beate; Moeller, Peter; Schadendorf, Dirk; Neubauer, Andreas; Huhn, Dieter; Schmidt-Wolf, Ingo G.H.
CORPORATE SOURCE: Department of Oncology and Hematology, Virchow-Klinikum, Humboldt-University, Berlin, 13353, Germany
SOURCE: Cancer Gene Ther. (1997), 4(4), 260-268
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Appleton & Lange
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with metastatic melanoma have a very poor prognosis. In many cases, the tumor recurs after surgical excision. Therefore, it might be beneficial for cancer patients to induce an immune attack against the tumor by inserting a cytokine gene into the tumor cells. Here, 14 primary cell cultures could be established from 45 patients with malignant melanoma. Primary cell cultures were transfected via electroporation with the gene encoding for human interleukin-7 (IL-7). Transfection resulted in the prodn. of biol. active IL-7 with an av. of 850 pg/mL per 106 cells per 24 h. Irradn. with 10,000 cGy, which inhibited tumor cell growth in vitro, increased the amt. of released IL-7 to an av. amt. of 1050 pg/mL per 106 cells per 24 h. No significant differences in the phenotype were obsd. in the IL-7-transfected cells compared with nontransfected cells. The expression of HLA class 1 and II, ICAM-1, and of a melanoma-assocd. antigen remained unaltered. Transfection with IL-7 had no significant effect on the proliferation of melanoma cells as measured in a MTT assay. There was no significant change in the cytokine profile after transfection or irradn. of the cells, but one cell culture expressed a high amt. of IL-6 (about 2 ng/mL). IL-6 was expressed in nontransfected cells and was not altered by transfection. Interestingly, transfected cells from primary melanoma cultures possessed a higher sensitivity to immunol. effector cells compared with nontransfected cells. This was true for allogeneic as well as autologous melanoma cells. The results show the feasibility of a gene transfer into primary human melanoma cells, different from retroviral transduction. IL-7-transfected cells might be of value in vaccination protocols for melanoma patients.

L163 ANSWER 26 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:506722 CAPLUS
DOCUMENT NUMBER: 125:192909
TITLE: Human dendritic cells genetically engineered to express high levels of the human epithelial tumor antigen mucin (MUC-1)
AUTHOR(S): Henderson, Robert A.; Nimgaonkar, Maya T.; Watkins, Simon C.; Robbins, Paul D.; Ball, Edward D.; Finn, Olivera J.
CORPORATE SOURCE: Dep. Med., Univ. Pittsburgh Sch. Med., Pittsburgh, PA, 15261, USA
SOURCE: Cancer Res. (1996), 56(16), 3763-3770
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The authors have achieved stable high-level expression of a human tumor antigen, epithelial cell mucin (MUC-1), on human dendritic cells (DCs) by retroviral transduction of CD34+ progenitor cells and their subsequent cytokine-induced differentiation into DCs. The process of retroviral transduction did not alter the growth or differentiation of DCs from CD34+ progenitor cells. Immunofluorescence and electron microscopy studies revealed that the expression of mucin was limited to the body of the DCs and was excluded from the cytoplasmic veils of the DCs. Furthermore, the expression of mucin on DCs was similar, if not identical, to the nonpolarized expression of mucin found on carcinoma cells. In functional studies, the MUC-1+-transduced DCs were potent stimulators of allogeneic CD4+ T cells and, in fact, were superior to MUC-1- DCs. Thus, MUC-1+ DCs are expected to be a valuable tool in the immunotherapeutic treatment of patients with tumors that express MUC-1.

L163 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:895373 CAPLUS
DOCUMENT NUMBER: 123:312189
TITLE: A B7-1-transfected human melanoma line stimulates proliferation and cytotoxicity of autologous and **allogeneic lymphocytes**
AUTHOR(S): Sule-Suso, Josep; Arienti, Flavio; Melani, Cecilia; Colombo, Mario Paolo; Parmiani, Giorgio
CORPORATE SOURCE: Div. Experimental Oncology D, Ist. Nazionale Tumori, Milan, Italy
SOURCE: Eur. J. Immunol. (1995), 25(10), 2737-42
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B7 co-stimulation is necessary to activate resting T cells upon antigen recognition by the T cell receptor. To see whether expression of B7 may render human melanoma cells able to stimulate T cells, a cloned melanoma line (Me1B6), which did not express B7-1, was transfected with the human B7-1 gene. In proliferation assays, B7-1 transfected cells (Me1B6/B7) showed greater stimulatory activity of allogeneic and autologous peripheral blood lymphocytes (PBL) compared to parental, non-transfected tumor cells. This effect was also seen when allogeneic CD8+ and CD4+ subpopulations were used as effectors. In these studies, **activation** of **lymphocytes** was B7-1-dependent and HLA classes I and II mediated. The higher proliferation correlated with an increased lytic activity by PBL stimulated with B7-1+ tumor cells against the untransfected Me1B6. Furthermore, PBL from a metastatic melanoma patient stimulated by Me1B6/B7 developed an higher lytic activity not only against Me1B6 but also against their autologous, B7-1- tumor. Finally, after Me1B6/B7 stimulation, PBL released interleukin (IL)-2 and interferon-.gamma., but not IL-4, suggesting a Th1-mediated response. These data support the use of B7-1 transfected melanoma cells in the therapeutic vaccination of melanoma patients.

L163 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:260263 CAPLUS
DOCUMENT NUMBER: 122:29689
TITLE: Induction of alloreactive cytotoxic T **lymphocytes** by intra-splenic immunization with **allogeneic** class I major histocompatibility complex DNA and DC-chol cationic liposomes
AUTHOR(S): Hui, Kam M.; Sabapathy, Tr. Kanaga; Oei, Audrey A.; Singhal, Arun; Huang, Leaf
CORPORATE SOURCE: Institute of Molecular and Cell Biology, National University of Singapore, Singapore, 0511, Singapore
SOURCE: J. Liposome Res. (1994), 4(3), 1075-90
CODEN: JLREE7; ISSN: 0898-2104

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple strategy for designing a cancer immunotherapeutic system involves modification of tumor cells from tumor-bearing animals in vivo in such a way that the host can evoke a specific immune response against them. We have expressed allogeneic class I major histocompatibility complex (MHC) mols. on tumor cells, through ex vivo DNA-mediated gene transfer. These mols. are potent immuno-modulators for the stimulation of strong immune reactions against certain malignancies. In order to achieve efficient gene delivery to tumor cells in vivo, we have compared the efficiencies of gene transfer into mammalian tumor cells by the biolistic particle delivery system and cationic liposomes. In this report, we have demonstrated that cationic liposomes prepd. by DC-chol and DOPE gives the best efficiency of transfection for tumor cells in vivo. We also showed that a strong anti-H-2Kb allo-reactive cytotoxic T lymphocyte (CTL) response could be generated following in vivo immunization of AKR/J mouse spleens with the H-2Kb gene and DC-chol cationic liposomes. The direct immunization of mouse spleens to induce cell-mediated immunity against exogenous antigens may allow alternative treatment strategies for cancer immunotherapy.

L163 ANSWER 29 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2001:448583 BIOSIS
DOCUMENT NUMBER: PREV200100448583
TITLE: Cancer immunotherapy using tumor cells combined with mixed lymphocytes.
AUTHOR(S): Hiserodt, John C. (1); Thompson, James A.; Granger, Gale A.
CORPORATE SOURCE: (1) Huntington Beach, CA USA
ASSIGNEE: The Regents of the University of California
PATENT INFORMATION: US 6207147 March 27, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 27, 2001) Vol. 1244, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB This invention comprises cellular **vaccines** and methods of using them in cancer **immunotherapy**, particularly in humans. The **vaccines** comprise **stimulated lymphocytes** **allogeneic** to the subject being treated, along with a source of tumor-associated antigen. The allogeneic lymphocytes can be stimulated by combining or coculturing them with leukocytes obtained from the subject to be treated or from another third-party donor. Tumor antigen may be provided in the form of primary tumor cells, tumor cell lines or tumor extracts prepared from the subject. Stimulated allogeneic lymphocytes and tumor antigen are combined and administered at a site distant from the primary tumor, in order to prime or boost a systemic cellular anti-tumor immune response. This approach overcomes the natural refractory nature of the immune system to stimulation by tumor antigens, generating a host response and potentially improving the clinical outcome.

L163 ANSWER 30 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2001:387988 BIOSIS
DOCUMENT NUMBER: PREV200100387988
TITLE: Simultaneous transduction of B7-1 and IL-2 genes into human melanoma cells to be used as **vaccine**: Enhancement of **stimulatory** activity for autologous and **allogeneic lymphocytes**.
AUTHOR(S): Mazzocchi, Arabella; Melani, Cecilia; Rivoltini, Licia; Castelli, Chiara; Del Vecchio, Michele; Lombardo, Claudia; Colombo, Mario P.; Parmiani, Giorgio (1)
CORPORATE SOURCE: (1) Unit of Immunotherapy of Human Tumors, Istituto Nazionale Tumori, Via Venezian 1, 20133, Milan:

parmiani@istitutotumori.mi.it Italy
SOURCE: Cancer Immunology Immunotherapy, (June, 2001) Vol. 50, No. 4, pp. 199-211. print.
ISSN: 0340-7004.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In order to construct an immunogenic cellular vaccine, we transduced three HLA-A*0201 human melanoma lines, selected for expression of classes I and II HLA, adhesion molecules and the T cell-defined melanoma antigens Melan/MART-1, gp100 and tyrosinase, with both interleukin-2 (IL-2) and B7-1 genes by the use of a polycistronic retroviral vector. The lines were selected to share only the HLA-A*0201 allele to avoid generation of strong alloreactivity in case of their multiple in vivo use in HLA-A*0201 + patients. Phenotypic and functional analysis of B7-1-IL2 transduced melanoma lines in comparison with B7-1 transduced and/or parental untransduced counterparts were then carried out. Tumor cells expressing either B7-1 or both genes did not change their original antigenic profile. From a functional point of view, expression of both genes in melanoma lines: (1) improved the response of anti-melanoma cytotoxic T lymphocytes (CTL) over singly transduced or untransduced melanoma cells when subthreshold levels of MHC-peptide complexes were expressed by melanoma cells; (2) conferred a distinct advantage in the ability to stimulate cytotoxicity and interferon-gamma release by autologous and/or HLA-A*0201-compatible allogeneic lymphocytes; (3) allowed the generation of a high number of specific CTL by in vitro stimulation of lymphocytes of HLA-A*0201-melanoma patients. Thus, B7-IL2 gene-transduced melanoma lines appear to display a high immunogenicity and could be used as vaccine in melanoma patients.

L163 ANSWER 31 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1998:513319 BIOSIS
DOCUMENT NUMBER: PREV199800513319
TITLE: Autologous and allogenic hybrid cell vaccine in patients with metastatic renal cell carcinoma.
AUTHOR(S): Kugler, A. (1); Seseke, F.; Thelen, P.; Kallerhoff, M.; Mueller, G. A.; Stuhler, G.; Mueller, C.; Ringert, R.-H.
CORPORATE SOURCE: (1) Klin. Urol., Georg August Univ., Robert-Koch-Str. 40, 37075 Goettingen Germany
SOURCE: BJU, (Oct., 1998) Vol. 82, No. 4, pp. 487-493.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Objective. To evaluate the safety, acute and long-term toxicity and therapeutic activity of an allogenic and an autologous hybrid cell vaccine in patients with progressive metastatic renal cell carcinoma (RCC). Patients and methods. Eleven patients were vaccinated with a lethally irradiated hybrid cell vaccine of allogenic RCC tumour cells fused with major histocompatibility complex class I-matched and class II-unmatched **activated allogenic lymphocytes**. These patients were then followed for a mean of 11 months. Another 13 patients were **vaccinated** with a hybrid cell **vaccine** of autologous tumour cells fused with **allogenic activated lymphocytes** and followed for a mean of 6 months. Results. Six of the 11 patients receiving the allogenic vaccination showed an initial response, with two complete and two partial responses to date. Only three patients who received autologous vaccination responded to treatment. Conclusions. Hybrid cell vaccination is a promising new approach in the treatment of patients with advanced RCC.

L163 ANSWER 32 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1991:528534 BIOSIS
DOCUMENT NUMBER: BA92:139994
TITLE: A POSSIBLE MECHANISM OF IMMUNOTHERAPY FOR PATIENTS WITH

RECURRENT SPONTANEOUS ABORTIONS.
AUTHOR(S): SUGI T; MAKINO T; MARUYAMA T; KIM W K; IIZUKA R
CORPORATE SOURCE: DEP. OBSTET. GYNECOL., SCH. MED., KEIO UNIV., 35 SHINANO-MACHI, SHINJUKU-KU, TOKYO 160, JPN.
SOURCE: AM J REPROD IMMUNOL, (1991) 25 (4), 185-189.
CODEN: AJRIE8.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The mechanism of the beneficial effect of immunotherapy for human reproductive wastage remains to be elucidated. Induction of blocking antibodies such as anti-HLA class II antibodies and anti-idiotypic antibodies was investigated as the mechanism of specific immunosuppression in pregnancy. We reported the changes in the mixed lymphocyte reaction (MLR), T-cell subsets, and generation of anti-idiotypic antibodies after immunotherapy compared to before immunotherapy. MLR was significantly ($P < 0.001$) inhibited after the immunization. The mean inhibition rate was 50.2%, suggesting that MLR blocking antibodies were induced by **immunotherapy**. Binding of autoantibodies to **alloactivated** maternal lymphoblasts against the paternal **lymphocytes** was detected in postimmunization cases in two-color flow-cytometric experiments. This suggests that anti-idiotypic antibodies were induced by the immunotherapy. The percentage of cytotoxic T-cells was significantly decreased ($P < 0.05$) and the percentage of suppressor T-cells was significantly increased ($P < 0.01$) after the immunotherapy, suggesting that a cell-mediated immune response was induced by the immunotherapy.

L163 ANSWER 33 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 1980:129224 BIOSIS
DOCUMENT NUMBER: BA69:4220
TITLE: CYTOSTATIC EFFECT ON TUMOR CELLS INDUCED IN HUMAN MONOCYTES BY MEDIATORS FROM BCG STIMULATED LYMPHOCYTES AND MIXED LYMPHOCYTE CULTURE.
AUTHOR(S): UNSGAARD G; HAMMERSTROM J; LAMVIK J
CORPORATE SOURCE: SECT. HAEMATOL. IMMUNOL., DEP. MED., TRONDHEIM REG. HOSP., N-7000 TRONDHEIM, NORW.
SOURCE: ACTA PATHOL MICROBIOL SCAND SECT C IMMUNOL, (1979) 87 (3), 159-166.
CODEN: APSCD2. ISSN: 0304-1328.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Human monocytes activated by mediators (lymphokines) from BCG-stimulated, sensitized lymphocytes (from BCG-**vaccinated** donors) were cytostatic to a human [NHiK 3025 cervical carcinoma] cell line. Mediators from **allogeneic lymphocytes activated** the cytostatic ability of monocytes to the same degree as mediators from autologous lymphocytes. Mediators from BCG-stimulated lymphocytes from tuberculin-negative donors not vaccinated with BCG, activated the monocytes only to a small extent. Culture of lymphocytes in a membrane chamber (MC) proximate to monocytes, or incubation of monocytes with filtered supernatants of lymphocyte cultures, were equally effective procedures for inducing cytostatic ability in monocytes. Supernatants of sensitized lymphocytes cultured with BCG for 4 h did not activate the monocytes, while supernatants collected after 24 h activated the cytostatic ability to the same extent as 72-h supernatants. Supernatants of mixed lymphocyte cultures (MLC) collected after 24 h did not activate the monocyte cytostatic ability at all. Supernatants (48 h and 72 h) of MLC showed a small but increasing activity. There was no significant difference between BCG-stimulated lymphocytes and MLC in their maximum DNA synthesis or in the kinetics of their DNA synthesis. The DNA synthesis and secretion of lymphocyte mediators may be independent phenomena resulting from the same stimulus.

L163 ANSWER 34 OF 49 BIOSIS COPYRIGHT 2002 BIOSIS

ACCESSION NUMBER: 1978:116095 BIOSIS
DOCUMENT NUMBER: BA65:3095
TITLE: STIMULATION OF HUMAN LYMPHOCYTES IN-VITRO BY LEUKOCYTES FROM PATIENTS WITH UNTREATED ACUTE MYELOID LEUKEMIA.
AUTHOR(S): TAYLOR G M; JONES S V; RIDWAY J C; HARRIS R
CORPORATE SOURCE: DEP. MED. GENET., ST. MARY'S HOSP., HATHERSAGE RD., MANCHESTER M13 OJH, ENGL., UK.
SOURCE: CLIN EXP IMMUNOL, (1977) 29 (2), 229-239.
CODEN: CEXIAL. ISSN: 0009-9104.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Leukocytes from 16 untreated acute myeloid leukemia (AML) patients were tested for their ability to stimulate lymphocytes from each of 12 normal donors. Of 192 tests between the stimulating AML leukocytes and responding lymphocytes, 42% resulted in positive lymphocyte stimulation; this was in contrast to 1-way mixed lymphocyte culture (MLC) responses, involving the same lymphocyte donors, which were 100% positive. Lack of stimulation by AML leukocytes was significantly associated, in 11% of the tests, with .gtoreq. 2 HL-A-A and/or-B antigens common to the responding lymphocyte and stimulating AML leukocyte. The most stimulatory of the AML leukocytes were obtained from 2 high-leukocyte-count acute myelomonocytic leukemia patients. The stimulatory capacity of AML leukocytes did not correlate with the clinical fate of the cell donor. The presence of contaminating lymphocytes from the patient in the AML leukocyte samples did not account for differences in stimulatory capacity between AML leukocytes. Limited in vitro viability of AML leukocytes was ruled out as a factor causing poor lymphocyte stimulation. Kinetic studies showed that AML leukocytes induce an MLC-type response or no response at all. Differences in response kinetics were observed between 2 normal and 2 remission AML patients, the latter receiving active immunotherapy. Pronase treatment of AML leukocytes failed to increase their stimulatory capacity, but distilled H2O markedly reduced it. The significance of results is discussed in relation to **lymphocyte stimulation** by other types of **allogeneic** cell and in the context of active **immunotherapy** of AML.

L163 ANSWER 35 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87060850 EMBASE
DOCUMENT NUMBER: 1987060850
TITLE: Control of human melanoma growth in nude mice by autologous allo-**activated** peripheral blood **lymphocytes**.
AUTHOR: Balsari A.; Tona G.; Colombo M.P.; et al.
CORPORATE SOURCE: Institute of Medical Microbiology, University of Milan, Milan, Italy
SOURCE: International Journal of Cancer, (1986) 38/6 (923-927).
CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
025 Hematology
LANGUAGE: English

AB Human peripheral blood **lymphocytes** (PBL) were **activated** in vitro by means of a pool of **allogeneic** PBL from normal donors and then evaluated for in vivo activity against human melanoma cells xenografted in splenectomized and irradiated athymic (nude) mice. The subcutaneous (s.c.) growth of human melanoma cells was inhibited by intravenous (i.v.) injection, 2 hr later, of such allo-activated, autologous and **allogeneic** PBL in 7/8 and in 6/9 mice respectively. Unstimulated PBL were ineffective. When allo-**activated** patients' **lymphocytes** were administered 3 days

after s.c. implantation of autologous melanoma cells, inhibition of tumor growth was observed in 1/6 mice. A significant delay in tumor appearance was noted in the remaining animals. Unstimulated as well as allo-activated, lymphokine-releasing helper-enriched human PBL had no effect on melanoma xenografts, indicating that the tumor inhibition by tumor-cytotoxic allo-activated PBL was not due to recruitment of murine immuno-competent cells by human lymphokines. These results indicate that allo-stimulated tumor-cytotoxic human PBL given i.v. to nude mice can circulate and inhibit the growth of autologous or **allogeneic** human melanoma cells implanted s.c.

L163 ANSWER 36 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87024113 EMBASE
DOCUMENT NUMBER: 1987024113
TITLE: Infusion of autologous **alloactivated** lymphocytes in melanoma patients: Toxicity and immunologic monitoring.
AUTHOR: Gambacorti-Passerini C.; Marolda R.; Tona G.; et al.
CORPORATE SOURCE: Divisione di Oncologia Sperimentale D, Istituto Nazionale Tumori, 20133 Milano, Italy
SOURCE: Tumori, (1986) 72/4 (383-388).
CODEN: TUMOAB
COUNTRY: Italy
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
016 Cancer
LANGUAGE: English

L163 ANSWER 37 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86099123 EMBASE
DOCUMENT NUMBER: 1986099123
TITLE: Systemic administration of autologous, **alloactivated** helper-enriched lymphocytes to patients with metastatic melanoma of the lung. A phase I study.
AUTHOR: Balsari A.; Marolda R.; Gambacorti-Passerini C.; et al.
CORPORATE SOURCE: Institute of Medical Microbiology, University of Milan, Milan, Italy
SOURCE: Cancer Immunology Immunotherapy, (1986) 21/2 (148-155).
CODEN: CIIMDN
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
016 Cancer
026 Immunology, Serology and Transplantation
013 Dermatology and Venereology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
AB A phase I study was carried out to test the feasibility and toxicity of infusing large numbers of autologous, **alloactivated** helper lymphocytes into patients with metastatic melanoma. Patient peripheral blood lymphocytes (Pt-PBL) obtained by lymphopheresis and expressing the helper phenotype BT5/9 were separated and stimulated for 48 or 72 h with a pool of PBL from four to six healthy donors. Patients were then infused with such activated lymphocytes over a 2-3 h period. A total of 4 phereses and infusions (2/week for 2 weeks) were carried out for each cycle in each patient. Of the five patients treated, two received a second round of infusions. Infusion of autologous PBL stimulated in vitro for 48 h caused chills, fever, headache, and increased blood pressure. All symptoms disappeared in 2-3 h and were easily controlled by appropriate therapy. When lymphocytes were given after 72 h of allostimulation, no or very mild toxicity was observed. Serum chemistry, coagulation, autoimmunity, and

urine analysis showed no gross abnormalities during therapy or follow-up of the patients. Immunological parameters (OKT4/OKT8 ratio, NK activity and cytotoxic T cell activity to autologous melanoma) were evaluated before starting the therapy, during its course and during the 3 to 6 months follow-up. The OKT4/OKT8 ratio increased significantly but transiently soon after the first course of infusions in one of the two patients tested. NK activity increased after 75-100 days in the three patients tested and in one of them it was high even after 180 days. No correlation between NK activity and prognosis was apparent. Cytotoxicity to autologous tumor was assessed in two patients, only one of whom exhibited an increased activity from 75 to 180 days, which was associated with a prognosis better than that of the negative patient. Five patients were treated: two had progressive disease, two had stable disease for 5 and 6 months, respectively. In the first of these patients, a new cycle of lymphocyte infusion was carried out which caused a measurable reduction of lung tumor nodules whose growth, however, resumed 4 months later. This patient died 14 months after the onset of therapy. The fifth patient had a partial regression of pulmonary and intracranial metastases after therapy, but eventually died 3 months later. These results indicate that infusion of a high numbers of autologous, allostimulated helper PBL is a feasible and safe procedure, which could therefore be used in future studies of adoptive immunotherapy of cancer.

L163 ANSWER 38 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86088668 EMBASE
DOCUMENT NUMBER: 1986088668
TITLE: In vitro killing of human glioblastoma by interleukin-2-**activated** autologous **lymphocytes**.
AUTHOR: Jacobs S.K.; Wilson D.J.; Kornblith P.L.; Grimm E.A.
CORPORATE SOURCE: Surgical Neurology Branch, National Institute of Neurological and Communicative Diseases, Disorders and Stroke, National Institutes of Health, Bethesda, MD, United States
SOURCE: Journal of Neurosurgery, (1986) 64/1 (114-117).
CODEN: JONSAC
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
AB Culture of peripheral blood lymphocytes (PBL) from brain-tumor patients with recombinant interleukin-2 (IL-2) results in the activation of lymphokine-activated killer cells (LAK) with the capacity to lyse autologous and **allogeneic** glioblastoma. In this study, PBL obtained from brain-tumor patients were cultured with or without IL-2 for 3 to 7 days and then tested for their ability to lyse target cells in a 4-hour chromium release cytotoxicity assay. The PBL were drawn 1 to 2 weeks following operative tumor debulking. Ceels used as targets included fresh brain-tumor cells obtained at the time of craniotomy, fresh brain-tumor cells grown from 1 to 3 weeks in tissue culture, fresh autologous PBL, and **allogeneic** glioblastoma cells grown in tissue culture. Peripheral blood lymphocytes from brain-tumor patients that were cultured without IL-2 did not significantly lyse autologous or **allogeneic** glioblastoma. However, when these PBL were cultured with IL-2, LAK were generated which produced marked lysis of autologous as well as **allogeneic** tissue-culture glioblastoma in all of eight cases. Significant lysis of autologous fresh tumor by patient LAK was observed in four of five experiments. By contrast, patient LAK did not kikk autologous normal PBL. The ability to generate LAK was not influenced by the patient's age, previous therapy, or the administration of steroids.

L163 ANSWER 39 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 85192275 EMBASE
DOCUMENT NUMBER: 1985192275
TITLE: Activation of human blood lymphocytes and monocytes by the streptococcal preparation OK432: Enhanced generation of soluble cytotoxic factors.
AUTHOR: Uchida A.; Klein E.
CORPORATE SOURCE: Department of Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
SOURCE: Immunology Letters, (1985) 10/3-4 (177-181).
CODEN: IMLED6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
030 Pharmacology
006 Internal Medicine
LANGUAGE: English
AB The streptococcal preparation OK432 augments natural cytotoxicity of human blood lymphocytes and monocytes. It also enhanced the production of natural killer soluble cytotoxic factors (NKCF) when the effector cells interact with K562 cells. There was a good correlation between the OK432-induced enhancement of NK cell-mediated cytotoxicity and the released NKCF activity. OK432-pretreated monocytes secreted higher amounts of monocyte cytotoxic factors (MCF) than the untreated monocytes. With the monocytes the enhanced generation of MCF was not always accompanied by the increase in direct cell-mediated lysis of K562. OK432 treatment alone did not induce NKCF release from lymphocytes, and the presence of K562 in the culture was necessary. In contrast, monocytes generated MCF when exposed to OK432. In the supernatants of cocultures of OK432-activated effectors and K562 the NKCF and MCF activity was elevated two- to ten-fold. The OK432-induced augmentation of natural cytotoxicity exerted by lymphocytes and monocytes may be mediated through an increase in the synthesis, activation and/or release of NKCF and MCF.

L163 ANSWER 40 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84243027 EMBASE
DOCUMENT NUMBER: 1984243027
TITLE: Immunological observations before and after successful treatment of chronic mucocutaneous candidiasis with ketoconazole and transfer factor.
AUTHOR: Corbeel L.; Ceuppens J.L.; Van Den Berghe G.; et al.
CORPORATE SOURCE: Department of Pediatrics, University of Leuven, B-3000 Leuven, Belgium
SOURCE: European Journal of Pediatrics, (1984) 143/1 (45-48).
CODEN: EJPEDT
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
026 Immunology, Serology and Transplantation
004 Microbiology
013 Dermatology and Venereology
LANGUAGE: English
AB A girl, 13 months of age, presented with generalised granulomatous skin, hair and mucosal candidiasis. Her lymphocytes failed to respond in vitro to Candida antigen (CA); the intradermal test with CA was also negative. Serum immunoglobulins, complement components, granulocyte functions (phagocytic and fungicidal), T-cell subsets, mitogenic and **allogenic lymphocyte stimulation**, natural killer cell activity and immune interferon production were all found to be normal. No circulating immune complexes were detected. Ketoconazole, an antimycotic drug, 5 mg/kg twice daily for 1 month and 2.5 mg/kg twice

daily for another month spectacularly cleared all lesions. Afterwards, 4-monthly injections with transfer factor (TF) were given. Intradermal reactivity to CA was observed after the second TF injection. The lymphocyte responsiveness to CA in vitro became strongly positive 3 months after the last TF injection. The level of CA precipitins in serum, which was very high (11 lines) before ketoconazole treatment, decreased to 4 lines. No serum inhibitor of lymphocyte proliferation to CA could be demonstrated in the patient's serum before or after treatment. This specific CA unresponsiveness was not due to an excess of OKT8 + (suppressor) cells; macrophage migration inhibiting factor (MIF) production was normal. The non-responsiveness might be due to antigenic overload or to suppressor cell induction not demonstrable in the present studies. The child has remained free of lesions during 3 years of follow-up without any further treatment.

L163 ANSWER 41 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84037049 EMBASE
DOCUMENT NUMBER: 1984037049
TITLE: Lysis of fresh natural killer-resistant tumor cells by lectin-activated syngeneic and **allogeneic** murine splenocytes.
AUTHOR: Mazumder A.; Rosenstein M.; Rosenberg S.A.
CORPORATE SOURCE: Surgery Branch, National Cancer Institute, NIH, Bethesda, MD 20205, United States
SOURCE: Cancer Research, (1983) 43/12 I (5729-5734).
CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
AB This paper demonstrates that lectin-**activated** **lymphocytes** of selected mouse strains can lyse fresh autologous or **allogeneic** tumor cells but not the fresh normal cells tested in short-term 51Cr release assays. Murine splenocytes, incubated with concanavalin A for 3 days, lysed tumor cells from fresh syngeneic P815 mastocytoma, 102 methylcholanthrene sarcoma, and FBL3 lymphoma; fresh **allogeneic** 3LL lung carcinoma and MethA sarcoma; and tissue-cultured YAK cells in 18-hr 51Cr release assays. Natural killer cells in fresh splenocyte preparations only lysed tissue-cultured YAK cells and not the other targets. Syngeneic and **allogeneic** lymphoblasts, lung, or liver cells were not lysed by the concanavalin A-activated killer (CAK) cells. The induction of cytotoxicity by concanavalin A incubation was abrogated by .alpha.-methylmannoside in the 3-day incubation, but not in cytotoxicity assay. Radiosensitive cells and adherent cells were necessary for the generation of CAK cells. The CAK effectors themselves were radioresistant, nonadherent, and mostly Thy 1+ and Ly 2+. The CAK phenomenon may be mediated by lymphokine production by an Ly 1+ cell, since depletion of Ly 1+ cells prior to activation abrogates CAK induction, and the ability of numerous mouse strains (and nude mice) to generate CAK cells correlated with their ability to produce Interleukin 2. The biological and therapeutic role of these cells is currently being investigated in murine sygeneic primary and metastatic tumor models.

L163 ANSWER 42 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81176446 EMBASE
DOCUMENT NUMBER: 1981176446
TITLE: PHA-**stimulated** **lymphocytes** injection therapy for advanced digestive cancer.
AUTHOR: Shimizu N.; Izumi A.; Kanayama H.; et al.
CORPORATE SOURCE: I Dept. Surg., Tottori Univ. Sch. Med., Yonago, Japan
SOURCE: Journal of Japan Society for Cancer Therapy, (1981) 16/2

(177-182).
CODEN: NGCJAK
COUNTRY: Japan
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
016 Cancer
026 Immunology, Serology and Transplantation
048 Gastroenterology
009 Surgery
LANGUAGE: Japanese
SUMMARY LANGUAGE: English

L163 ANSWER 43 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81155210 EMBASE
DOCUMENT NUMBER: 1981155210
TITLE: Heavy metal modulation of lymphocyte activities-II. Lead, and in vitro mediator of B-cell activation.
AUTHOR: Lawrence D.A.
CORPORATE SOURCE: Dept. Microbiol. Immunol., Albany Med. Coll. Un. Univ., Albany, N.Y. 12208, United States
SOURCE: International Journal of Immunopharmacology, (1981) 3/2 (153-161).
CODEN: IJIMDS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
025 Hematology
023 Nuclear Medicine
030 Pharmacology
026 Immunology, Serology and Transplantation
LANGUAGE: English
AB Investigation of the immunopotentiating effect(s) of Pb2+ on the humoral immune response has provided evidence that a heavy metal can alter the proliferation and differentiation of B-cells. Pb2+ interacted with B-cells to enhance both their proliferation and their differentiation into sheep red blood cell (SRBC)-specific PFC. Preincubation of B-cells with Pb2+ for only 1 h enhanced their activities. Enhancement of in vitro humoral immunity to SRBC was due to direct Pb2+ activation of B-cells and enhancement of T-cell help. Furthermore, Pb2+ and the cyclic nuleotides dibutyryl cyclic adenosine monophosphate (DBcAMP) or cyclic guanosine monophosphate (cGMP) worked in a synergistic manner to enhance the B-cell proliferation, and Pb2+ and DBcAMP synergistically enhanced PFC development. Ni2+, which had been shown to enhance PFC development in cultures of spleen cells in a manner equivalent to Pb2+, did not enhance PFC development in B-cell cultures as well as Pb2+ and did not produce synergistic effects with DBcAMP or cGMP. The possible mechanisms by which Pb2+ enhances B-cell activities and the implications of these effects are discussed.

L163 ANSWER 44 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 79254007 EMBASE
DOCUMENT NUMBER: 1979254007
TITLE: [Action of isoprinosine on the 'in vitro' activation of human lymphocytes].
EFFETS DE L'ISOPRINOSINE SUR L'ACTIVATION DES LYMPHOCYTES HUMAINS IN VITRO.
AUTHOR: Morin A.; Griscelli C.; Daguillard F.
CORPORATE SOURCE: INSERM U 132, Hop. Necker-Enf. Mal., 75015 Paris, France
SOURCE: Annales d'Immunologie, (1979) 130/4 (541-551).
CODEN: ANIMCZ
COUNTRY: France
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
030 Pharmacology
LANGUAGE: French
SUMMARY LANGUAGE: English

L163 ANSWER 45 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78374278 EMBASE
DOCUMENT NUMBER: 1978374278
TITLE: A phase I study of active specific intralymphatic immunotherapy (ASILI).
AUTHOR: Juillard G.J.F.; Boyer P.J.J.; Yamashiro C.H.
CORPORATE SOURCE: Div. Radiat. Ther., Dept. Radiol. Sci., UCLA Sch. Med., Los Angeles, Calif., United States
SOURCE: Cancer, (1978) 41/6 (2215-2225).
CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
009 Surgery
LANGUAGE: English
AB Twenty-one patients with advanced malignancies who had exhausted or refused conventional modalities of treatment were entered in a Phase I toxicology trial of active specific intralymphatic immunotherapy (ASILI). The patients were immunized with 1 x 107 to 1.2 x 108 viable autochthonous or **allogeneic** irradiated tumor cells intralymphatically each month and received no other antineoplastic treatment. To date, 274 intralymphatic injections have been performed and except for one case of bacterial lymphangitis, no adverse side effects have been observed. ASILI did not significantly alter peripheral blood lymphocyte counts, absolute E-rosette forming cell levels, or EA-rosette forming cell levels. PHA reactivity of peripheral blood lymphocytes increased slightly in all but one patient tested. Seven out of nine patients who had not had delayed hypersensitivity to recall antigens developed positive reactions following ASILI. Sixteen out of twenty patients tested also developed reactivity to their immunizing cells after treatment. Objective regression (greater than 50% reduction of tumor mass) was observed in five out of nineteen evaluable patients. Six patients showed stabilization of tumor growth and eight patients continued to progress under treatment.

L163 ANSWER 46 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 79011967 EMBASE
DOCUMENT NUMBER: 1979011967
TITLE: In vitro induction of cell-mediated immunity to murine leukemia cells. V. Adoptive immunotherapy of leukemia in mice with lymphocytes sensitized in vitro to leukemia cells.
AUTHOR: Kedar E.; Schwartzbach M.; Hefetz S.; Raanan Z.
CORPORATE SOURCE: Lautenberg Cent. Gen. Tum. Immunol., Hebrew Univ., Hadassah Med. Sch., Jerusalem, Israel
SOURCE: Cancer Immunology Immunotherapy, (1978) 4/3 (151-159).
CODEN: CIIMDN
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
LANGUAGE: English
AB The present study was undertaken to evaluate the feasibility of adoptive immunotherapy of murine leukemias using lymphocytes specifically

sensitized in vitro to leukemia cells (EL4, YAC). Large numbers of **activated lymphocytes** of both syngeneic and **allogeneic** origin were generated in macro-mixed leukocyte-tumor cell cultures (MLTC) and their antitumor reactivity was assessed in vitro (51Cr release assay) and in vivo (Winn neutralization assay and immunotherapy of established leukemia). In the Winn assay, tumor-lymphocyte mixtures were administered by subcutaneous (s.c.), intraperitoneal (i.p.), or intravenous (i.v.) routes. Sensitized lymphocytes were highly effective in inhibiting tumor growth when given by the s.c. route, whereas they were much less so following administration by the other routes. There was a good correlation between the cytoxic potential in vitro and the tumor-neutralizing capacity in vivo. Syngeneic lymphocytes were more efficient than were **allogeneic** lymphocytes. In the immunotherapy experiments, cytotoxic lymphocytes (CL) were inoculated by different routes 24-48 hr after mice had been given a lethal dose of tumor cells. Although a significant retardation of tumor growth was achieved, complete cures were rare. These findings thus demonstrate that, under the conditions employed, CL generated in vitro and endowed in vitro with strong antitumor cytotoxicity have, by themselves, only a limited immunotherapeutic capacity in vivo.

L163 ANSWER 47 OF 49 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-277629 [23] WPIDS
CROSS REFERENCE: 1999-277438 [23]
DOC. NO. CPI: C1999-081664
TITLE: Increasing the level of cytokine secretion by **alloactivated** lymphocytes.
DERWENT CLASS: B04 D16
INVENTOR(S): THOMPSON, J A
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9919462	A1	19990422	(199923)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9897946	A	19990503	(199937)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9919462	A1	WO 1998-US21318	19981009
AU 9897946	A	AU 1998-97946	19981009

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9897946	A	Based on	WO 9919462

PRIORITY APPLN. INFO: US 1997-61662P 19971010
AB WO 9919462 A UPAB: 19990616
NOVELTY - A method for:
(a) increasing the level of cytokine secretion by;
(b) increasing the level of esterase activity in; or
(c) increasing the level of CD69 expression by,

alloactivated lymphocytes, comprises adding an H2 receptor antagonist to the medium of an ex vivo culture of responder **lymphocytes** and **allogeneic stimulator** cells, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIMS is also included for a method of preparing a cultured cell population containing **alloactivated** human donor lymphocytes for treating a tumor in a human patient, comprising:

(i) co-culturing human lymphocytes allogeneic to the human patient ex vivo with human leukocytes allogeneic to the lymphocytes so as to **alloactivate** the lymphocytes;

(ii) harvesting the co-cultured cells from culture at a time when the harvested cells, upon implantation in the bed of a solid tumor in the patient, are effective in the treatment of the tumor; and

(iii) preparing the harvested cells for human administration to be used in methods (a), (b) and (c).

ACTIVITY - Immunostimulant.

An interleukin-2 (Il-2) specific enzyme-linked immunosorbent assay was performed to quantitate the production of Il-2 in supernatants of cultured human peripheral blood mononuclear cells after 3 days at 37 deg. C in RPMI-2% fetal calf serum. Cells were cultured at the 10:1 ratio of responder (Donor A) to stimulator (Donor B), or vice-versa, in the presence or absence of 20 micro g/ml Cimetidine.

More interleukin was made by Donor B in response to A. Cimetidine raised the amount of II-2 secreted after 3 days in both mixed lymphocyte reactions.

MECHANISM OF ACTION - Histamine 2 receptor antagonism which inhibits the activity of suppressor T cells in the culture.

USE - The methods are useful in **immunotherapy** to treat or elicit an anti-tumor response to tumor cells selected from melanoma, pancreatic cancer, liver cancer, colon cancer, prostate cancer and breast cancer cells (all claimed).

ADVANTAGE - None given.

Dwg.0/5

L163 ANSWER 48 OF 49 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-322710 [28] WPIDS
DOC. NO. CPI: C1998-099335
TITLE: Maturation of dendritic cells from mono nuclear cells in vitro - useful as adjuvants for, e.g. treating tumours and infections by activation of T cell(s).
DERWENT CLASS: B04 D16
INVENTOR(S): CEBON, J S; LE THOMAS, E; LUFT, T; PANG, K
PATENT ASSIGNEE(S): (LUDW-N) LUDWIG INST CANCER RES
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9823728	A1	19980604	(199828)*	EN	84
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP US					
AU 9850415	A	19980622	(199844)		
EP 941309	A1	19990915	(199942)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
AU 718873	B	20000420	(200029)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9823728	A1	WO 1997-AU801	19971127
AU 9850415	A	AU 1998-50415	19971127

EP 941309	A1	EP 1997-913011	19971127
		WO 1997-AU801	19971127
AU 718873	B	AU 1998-50415	19971127

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9850415	A	Based on	WO 9823728
EP 941309	A1	Based on	WO 9823728
AU 718873	B	Previous Publ.	AU 9850415
		Based on	WO 9823728

PRIORITY APPLN. INFO: AU 1996-3883 19961127

AB WO 9823728 A UPAB: 19980715

Maturation of dendritic cells (DC) is induced in vitro by culturing mononuclear cells in serum-free medium in presence of a type I interferon (I), following an initial growth phase in presence of granulocyte-macrophage colony stimulating factor (GM-CSF), tumour necrosis factor alpha (TNFa) and interleukin-4 (IL-4). Also new are: (1) increasing antigen-presenting capacity of DC by treatment with (I); (2) population of mature DC that: (i) are non-phagocytic; (ii) have strong antigen-presenting activity; (iii) **stimulate** multiplication of **allogeneic lymphocytes** in a mixed **lymphocyte** reaction; (iv) **stimulate** autologous, peptide-specific cytotoxic T lymphocytes (CTL) in a mixed leucocyte peptide culture assay, and (v) are produced under serum-free conditions; (3) tumour-activated T cells activated by DC, and (4) cellular adjuvant produced by treating mature DC with a specific antigen.

USE - (I) may be used as adjuvants in **vaccines** against tumours and infectious agents (claimed). DC are used: (i) to prepare cellular adjuvants for treatment of neoplastic disease and infections (by bacteria, viruses, fungi or parasites), or (ii) to activate T cells from a tumour patient (for subsequent administration to the patient). The population of (2) is also used to treat such diseases, optionally administered with, or after, the appropriate antigen.

ADVANTAGE - The mature DC are powerful antigen-presenting cells for both allogeneic T cells and autologous, peptide-stimulated CTL, so stimulate anti-tumour or anti-pathogen responsesC are generated from CD34+ progenitor cells in absence of stem-cell expanding cytokines or other expensive additives.

Dwg.17B/20

L163 ANSWER 49 OF 49 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:	1989-206464 [28] WPIDS
DOC. NO. CPI:	C1989-091683
TITLE:	Lymphokine **activated** autologous or **allogenic lymphocytes** - used in adoptive **immuno therapy** to treat e.g. aids or its related complex.
DERWENT CLASS:	B04 C03 D16
INVENTOR(S):	SHARP, J C; SULTAN, A
PATENT ASSIGNEE(S):	(BROW-N) BROWNINGS CLINICAL
COUNTRY COUNT:	30

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8905657	A	19890629	(198928)*	EN	88
RW: AT BE CH DE FR GB IT LU NL OA SE					
W: AU BB BG BR DK FI HU JP KP KR LK MC MG MW NO RO SD SU US					
AU 8929257	A	19890719	(198941)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8905657	A	WO 1988-GB1134	19881219

PRIORITY APPLN. INFO: GB 1987-29410 19871217; GB 1988-17082 19880718; GB 1988-23895 19881012; GB 1988-23896 19881012; GB 1988-23897 19881012

AB WO 8905657 A UPAB: 19930923
Method for the activation of lymphocytes from a patient or donor for use in adoptive **immunotherapy**, is claimed, in which an autologous or allogenic (donor) lymphocyte contg. liq. is incubated with a lymphokine (I), and the resultant culture contg. the patient directly.

Also claimed is a compsn. of antibodies (Ab) capable of controlling and neutralising an infectious agent (II). The Abs are harvested from (I)s previously exposed to the agent.

USE - LAKs are used to treat oncological or infectious deseases, e.g. retroviruses such as AIDS and ARC. The process of reinfusion of LAK provides some clinical improvements, but it is time consuming and requires skilled lab. work. The method of the invention is greatly abbreviated thus making its benefits more generally available. The reinfusable, therapeutic compsn. is used in adoptive **immunotherapy** with patient-specific LAK cells. When a (I) is activated with a lymphokine, the number of binding sites for HIV (HIV) replicates by binding to CD4 receptor sites) is greatly increased so free viruses bind to activated (I)s rather than normal non-activated (I)s. This means the virus in the cell cannot replicate and is removed from circulation. LAKs increase suppressor cell activity and suppress a patient's ability to respond to foreign cells. This induces tolerance to foreign tissues and is used in transplants to reduce rejection, e.g. transplanting haematopoietic tissue and other organs such as kidneys, livers and hearts.
0/5

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=> fil capl; d que l34; d que l42; s (l34 or l42) not l161; fil cancer; d que l76; s l76
not l61
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FILE LAST UPDATED: 13 Jan 2002  (20020113/ED)

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L6          9219 SEA FILE=CAPLUS ABB=ON  ALLOGEN?
L7           112 SEA FILE=CAPLUS ABB=ON  ALLOACTIVAT?
L8           733 SEA FILE=CAPLUS ABB=ON  ANTIGENICALLY DISTINCT
L9        133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L10          742 SEA FILE=CAPLUS ABB=ON  L9(L)((L6 OR L7 OR L8))
L11        25426 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L13          516 SEA FILE=CAPLUS ABB=ON  L9(L)L11
L14            4 SEA FILE=CAPLUS ABB=ON  L13 AND L10
L15         5041 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CT OR THERAP?(L)IMMUNO/OB
                 I
L16           10 SEA FILE=CAPLUS ABB=ON  L10 AND L15
L17         1046 SEA FILE=CAPLUS ABB=ON  L9(L)(MIX##### OR COCULTUR? OR CO
                 CULTUR?)
L26            2 SEA FILE=CAPLUS ABB=ON  L17 AND L11 AND L15
L27       167362 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#
L28        28436 SEA FILE=CAPLUS ABB=ON  L27(3A)(ACTIVAT? OR L7 OR STIMULAT?)
L31            5 SEA FILE=CAPLUS ABB=ON  (L11 OR L15) AND L28 AND (L10 OR L17)
L32         7269 SEA FILE=CAPLUS ABB=ON  (TUMOUR OR TUMOR)(1W)ANTIGEN#
L33            9 SEA FILE=CAPLUS ABB=ON  L10 AND L32 AND L11
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L34          5 SEA FILE=CAPLUS ABB=ON  L33 NOT (L14 OR L16 OR L26 OR L31)


L9      133335 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#/OBI
L11      25426 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L15       5041 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CT OR THERAP?(L)IMMUNO/OB
               I
L27     167362 SEA FILE=CAPLUS ABB=ON  LYMPHOCYTE#
L35       3828 SEA FILE=CAPLUS ABB=ON  L27(2A)(MIX##### OR THIRD PARTY)
L39       2967 SEA FILE=CAPLUS ABB=ON  ANTIGEN#/CW(L)(TUMOR ASSOC?)
L40        493 SEA FILE=CAPLUS ABB=ON  L9 AND L39 AND (L11 OR L15)
L42          1 SEA FILE=CAPLUS ABB=ON  L40 AND L35


L164         5 (L34 OR L42) NOT L161
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previously printed

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FILE 'CANCERLIT' ENTERED AT 13:57:42 ON 14 JAN 2002

 FILE COVERS 1963 TO 14 Jun 2001 (20010614/ED)

 CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2000 vocabulary.  Enter HELP THESAURUS for details.

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L46      14703 SEA FILE=CANCERLIT ABB=ON  ALLOGEN?
L47        128 SEA FILE=CANCERLIT ABB=ON  ALLOACTIVAT?
L48        291 SEA FILE=CANCERLIT ABB=ON  ANTIGENICALLY DISTINCT
L49      18444 SEA FILE=CANCERLIT ABB=ON  LYMPHOCYTES/CT
L51       8343 SEA FILE=CANCERLIT ABB=ON  VACCINES+NT/CT
L52      22876 SEA FILE=CANCERLIT ABB=ON  IMMUNOTHERAPY+NT/CT
L57       6932 SEA FILE=CANCERLIT ABB=ON  L49(L)IM/CT
L70      39351 SEA FILE=CANCERLIT ABB=ON  ANTIGENS, NEOPLASM+NT/CT
L73       7876 SEA FILE=CANCERLIT ABB=ON  L70(L)IM/CT
L75      15252 SEA FILE=CANCERLIT ABB=ON  L70(L)AN/CT
L76          8 SEA FILE=CANCERLIT ABB=ON  (L57 AND L73 AND (L46 OR L47 OR
               L48) AND (L52 OR L51)) NOT L75
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Subheadings
IM - immunology
AN - analysis

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L165         8 L76 NOT L61

=> fil wpids;d que l100; s l100 not l89; fil embase; d que l149; s l149 not l162; fil
biosis; d que l159; s l159 not l160
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FILE LAST UPDATED: 09 JAN 2002              <20020109/UP>
MOST RECENT DERWENT UPDATE            200202   <200202/DW>
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L77 588 SEA FILE=WPIDS ABB=ON ALLOGEN?
L78 6 SEA FILE=WPIDS ABB=ON ALLOACTIVAT?
L79 5711 SEA FILE=WPIDS ABB=ON LYMPHOCYTE# OR LYMPHO CYTE#
L80 11 SEA FILE=WPIDS ABB=ON ANTIGENICALLY DISTINCT?
L93 307 SEA FILE=WPIDS ABB=ON (TUMOR OR TUMOUR)(W)ASSOC?(W)ANTIGEN#
L99 47 SEA FILE=WPIDS ABB=ON (L77 OR L78 OR L80)(5A)L79
L100 3 SEA FILE=WPIDS ABB=ON L99 AND L93

L166 3 L100 NOT (L89) previously printed

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L125 36705 SEA FILE=EMBASE ABB=ON LYMPHOCYTE/CT
L126 229 SEA FILE=EMBASE ABB=ON ALLOACTIVAT?
L127 25501 SEA FILE=EMBASE ABB=ON ALLOGEN?
L128 762 SEA FILE=EMBASE ABB=ON ANTIGENICALLY DISTINCT
L129 10806 SEA FILE=EMBASE ABB=ON TUMOR ANTIGEN/CT
L131 42929 SEA FILE=EMBASE ABB=ON IMMUNOTHERAPY+NT/CT
L132 13938 SEA FILE=EMBASE ABB=ON VACCINE/CT OR TUMOR VACCINE/CT OR TUMOR CELL VACCINE/CT OR CANCER VACCINE/CT
L139 2960 SEA FILE=EMBASE ABB=ON LYMPHOCYTE#(5A)(ACTIVAT? OR STIMULAT?) AND (L127 OR L128)
L141 8991 SEA FILE=EMBASE ABB=ON LYMPHOCYTE ACTIVATION/CT
L149 4 SEA FILE=EMBASE ABB=ON (L139 OR L126 OR L141) AND L125 AND (L131 OR L132) AND L129

L167 4 L149 NOT (L162) previously printed

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L150 234206 SEA FILE=BIOSIS ABB=ON LYMPHOCYTE#

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L151        210 SEA FILE=BIOSIS ABB=ON  ALLOACTIVAT?
L152      28996 SEA FILE=BIOSIS ABB=ON  ALLOGEN? OR ANTIGENICALLY DISTINCT
L153        794 SEA FILE=BIOSIS ABB=ON  L150(5A)L152(5A)(ACTIVAT? OR STIMULAT?)

L154         84 SEA FILE=BIOSIS ABB=ON  L150(5A)L151
L155      85371 SEA FILE=BIOSIS ABB=ON  VACCINE# OR VACCINAT?
L156      28855 SEA FILE=BIOSIS ABB=ON  IMMUNOTHERAP? OR IMMUNO THERAP?
L157         57 SEA FILE=BIOSIS ABB=ON  (L153 OR L154) AND (L155 OR L156)
L158       3709 SEA FILE=BIOSIS ABB=ON  (TUMOR OR TUMOUR)(W)ASSOC?(W)ANTIGEN#
L159          3 SEA FILE=BIOSIS ABB=ON  L157 AND L158

L168          2 L159 NOT L160   previously printed

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PROCESSING COMPLETED FOR L168
PROCESSING COMPLETED FOR L167
PROCESSING COMPLETED FOR L166
L169         21 DUP REM L165 L164 L168 L167 L166 (1 DUPLICATE REMOVED)
                ANSWERS '1-8' FROM FILE CANCERLIT
                ANSWERS '9-12' FROM FILE CAPLUS
                ANSWERS '13-14' FROM FILE BIOSIS
                ANSWERS '15-18' FROM FILE EMBASE
                ANSWERS '19-21' FROM FILE WPIDS

=> d ibib ab 1-21; fil hom

L169 ANSWER 1 OF 21  CANCERLIT                          DUPLICATE 1
ACCESSION NUMBER:    96225882  CANCERLIT
DOCUMENT NUMBER:     96225882
TITLE:               Protection against metastasis by immunization with an
                     allogeneic lymphocyte antigen.
AUTHOR:              Egawa K; Seo N; Tanino T; Tsukiyama T
CORPORATE SOURCE:    Department of Tumor Biology, University of Tokyo, Japan.
SOURCE:              CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1995). Vol. 41, No. 6,
                     pp. 384-8.
                     Journal code: CN3. ISSN: 0340-7004.
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT:        MEDL; L; Cancer Journals; Priority Journals
LANGUAGE:            English
OTHER SOURCE:        MEDLINE 96225882
ENTRY MONTH:         199608
AB   Q5 antigens are expressed on the surface of various experimental murine
     tumor cells. They share partially common antigenicity with Qa-2
     alloantigens expressed on normal lymphocytes. For that reason we tested
```

the immunoprotection by anti-Qa-2 immunization of mice against a Q5+ tumor. Nerve fibrosarcoma (NSFA) tumor, which specifically develops metastasis in the lung, has been reported to be poorly immunogenic. However, expression of the Q5 antigen was evident on the surface of NFSA cells. After immunizing (C3H/He x B6.K1)F1 (Qa-2-) mice with B6 (Qa-2+) lymphocytes, the protection against the proliferation of the semi-syngeneic NFSA tumor was examined. First, immunization of normal mice induced resistance to NFSA cell transplants. Second, when the tumor cells were transplanted to the hind foot of a mouse and the resulting tumor was removed by amputating the leg, the mice were protected against the development of lung metastasis after immunization by intraperitoneal inoculation of B6 cells 3 days after tumor removal. Immunization with attenuated NFSA cells in this system failed to protect the mice from lung metastasis. On the other hand, inoculation of the mice with B6 cells without removal of the original tumor on the foot showed little effect on the progression of the tumor. Thus, cytotoxic T lymphocytes (CTL), which seemed to be present in an inactive form in the mice from which the tumor had not been removed, were induced in the mice after the removal of the major tumor followed by immunization with B6 lymphocytes. The induction of CTL by the immunization was suppressed in mice bearing large tumors. Cells stimulated by the tumor antigen seemed to be involved in the suppression. It was also shown that the Q5 antigen is the direct recognition target of the CTL since the activity of Q5-specific CTL clones in lysing tumor cells was inhibited by a monoclonal antibody specific for the Q5 antigen. In contrast to immunization with attenuated tumor cells, our novel **allogeneic** lymphocyte immunization procedure offers high CTL activation, by-passing the induction of T cell unresponsiveness.

L169 ANSWER 2 OF 21 CANCERLIT
ACCESSION NUMBER: 89328458 CANCERLIT
DOCUMENT NUMBER: 89328458
TITLE: Induction of tumor-infiltrating lymphocytes in human malignant melanoma metastases by immunization to melanoma antigen vaccine.
AUTHOR: Oratz R; Cockerell C; Speyer J L; Harris M; Roses D; Bystryn J C
CORPORATE SOURCE: Department of Medicine, New York University School of Medicine, New York.
SOURCE: JOURNAL OF BIOLOGICAL RESPONSE MODIFIERS, (1989). Vol. 8, No. 4, pp. 355-8.
Journal code: JBM. ISSN: 0732-6580.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 89328458
ENTRY MONTH: 198910
AB We report a statistically significant increase in tumor-infiltrating lymphocytes in subcutaneous melanoma metastases removed from patients immunized with a melanoma vaccine. Dense cellular infiltrates were seen in 10 of 11 nodules from vaccine-immunized patients, compared with 9 of 22 nodules from non-immunized patients ($p = 0.02$). Furthermore, these dense lymphocytic collections more frequently infiltrated the body of tumor nodules from immunized patients, whereas in non-immunized patients, lymphocytes were more often present only in the dermal tissue at the periphery of the nodule. Thus, **allogeneic** melanoma vaccines may augment immune responses to a patient's own tumor.

L169 ANSWER 3 OF 21 CANCERLIT
ACCESSION NUMBER: 90359763 CANCERLIT
DOCUMENT NUMBER: 90359763
TITLE: Impaired induction of delayed hypersensitivity following anterior chamber inoculation of alloantigens.
AUTHOR: Williamson J S; Streilein J W

CORPORATE SOURCE: Department of Microbiology, University of Miami School of Medicine, FL 33101.
CONTRACT NUMBER: EY-05678 (NEI)
SOURCE: REGIONAL IMMUNOLOGY, (1988). Vol. 1, No. 1, pp. 15-23. Journal code: AVT. ISSN: 0896-0623.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 90359763
ENTRY MONTH: 199011

AB BALB/c mice that receive **allogeneic** P815 tumor cells (DBA/2 origin) into the anterior chamber of the eye (intracamerally, i.c.) fail to develop DBA/2-specific delayed hypersensitivity (DH). We have previously shown that this failure results, in part, from the generation of efferent T suppressor cells. To determine whether DH effector cells are even activated in these mice, a local adoptive transfer assay for DH was developed: Mixtures of responder lymphocytes and irradiated stimulator cells were injected into the pinnae of normal mice, syngeneic with the responders. In this assay, spleen cells from i.c. injected donors failed to evoke a local DH. Moreover, when spleen cells from i.c. injected donors were mixed with specifically immune BALB/c anti-DBA/2 lymphoid cells and similarly assayed, DH was effectively suppressed. Spleen cells from i.c. injected mice, depleted of Lyt-2+ suppressor cells, remained unresponsive in this assay, even if before injection they had been exposed to 5 days of in vitro culture with DBA/2 alloantigens. We conclude that anterior chamber inoculation of P815 cells in BALB/c mice fails to activate DH effector cells. Therefore, the inability of i.c. injected mice to mount DH responses results not only from efferent suppression but also from selective impairment of DH induction. The latter effect may be due to the activation of an afferent suppressor mechanism that acts selectively on T cell help for DH but that has no effect on help for B cells or cytotoxic T cell precursors.

L169 ANSWER 4 OF 21 CANCERLIT
ACCESSION NUMBER: 86239832 CANCERLIT
DOCUMENT NUMBER: 86239832
TITLE: Immunoregulatory molecules of trophoblast and decidual suppressor cell origin at the maternofetal interface.
AUTHOR: Clark D A; Slapsys R; Chaput A; Walker C; Brierley J; Daya S; Rosenthal K L
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY AND MICROBIOLOGY, (1986). Vol. 10, No. 3, pp. 100-4. Journal code: 3XY. ISSN: 8755-8920.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 86239832
ENTRY MONTH: 198608

AB The mammalian fetus expresses a variety of paternal histocompatible, oncofetal, and trophoblast antigens against which the mother can mount an immune response. Survival of the "fetal graft" appears to depend upon local immunosuppressive mechanisms in lymph nodes draining the uterus and at the intrauterine implanation site itself. Nonspecific not-T-Fc-receptor-bearing small lymphocytes containing cytoplasmic granules present in successfully allopregnant mice can suppress both the generation of maternal-antipaternal killer T cells and the infiltration of cytotoxic T lymphocytes into sponge-matrix allografts during the effector phase of the immune response. These suppressor cells are deficient at the implantation sites of xenogeneic and **allogeneic** mouse embryos that are susceptible to maternal immunity and are destined to resorb. A soluble suppressor factor of approximately 100,000 daltons in size can be obtained from the suppressor cells and acts to block the response of T cells to interleukin-2 by interfering with IL-2 receptors. The development

of the suppressor cells in the decidua requires certain hormonal signals as well as signals provided by trophoblast cells. Freshly explanted or cultured murine trophoblast cell lines elaborate soluble factor(s) that are active in recruitment or activation of suppressor cells. Since suppressor cells may be isolated from decidua of successfully allopregnant humans, the suppressor cell mechanism and its regulation may represent a key factor in the protection of the "fetal allograft" from rejection by maternal immunity.

L169 ANSWER 5 OF 21 CANCERLIT
ACCESSION NUMBER: 84091614 CANCERLIT
DOCUMENT NUMBER: 84091614
TITLE: The effects of syngeneic soluble tumor membrane extract on concomitant spleen cell immunity and spontaneous metastases.
AUTHOR: Temple W J; Sugarbaker E V; Ketcham A S
SOURCE: JOURNAL OF SURGICAL RESEARCH, (1984). Vol. 36, No. 1, pp. 71-9.
Journal code: K7B. ISSN: 0022-4804.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 84091614
ENTRY MONTH: 198403
AB The effects of a soluble tumor KCl extract, containing membrane antigen on spontaneous metastases and spleen cell immunity were studied in a syngeneic C57BL/6J murine sarcoma model. The extract was shown to be **antigenically distinct** from normal tissue by tumor immunization rejection experiments. Tumor soluble extract (SE) was administered daily during the growth of a murine sarcoma. The afferent and efferent arc of immunity were monitored by proliferative index (PI) and in vitro cytotoxicity of spleen cells, as well as the incidence of metastases. PI was significantly activated in the group receiving sarcoma SE as compared to the two control groups receiving muscle SE or saline P less than 0.05. However, in vitro cytotoxicity was significantly depressed on Days 7 and 14 (P less than 0.05) of tumor growth in the mice receiving sarcoma SE. The incidence of metastases was significantly increased to 70% in the sarcoma SE group as compared to the incidence in the control groups of 50% P less than 0.05. This data supports the hypothesis that release of soluble antigen membrane components by growing tumor facilitates the growth of metastases in this model.

L169 ANSWER 6 OF 21 CANCERLIT
ACCESSION NUMBER: 83157926 CANCERLIT
DOCUMENT NUMBER: 83157926
TITLE: Antigenic properties of human IgG Kappa and IgG lambda myeloma plasma cells.
AUTHOR: Hagner G
SOURCE: EXPERIMENTAL HEMATOLOGY, (1983). Vol. 11, No. 3, pp. 219-25.
Journal code: EPR. ISSN: 0301-472X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 83157926
ENTRY MONTH: 198306
AB In 12 patients with multiple myeloma of type IgG, lymphocytes were isolated from the peripheral blood and sensitized to a pool of normal **allogeneic** cells or to **allogeneic** or autologous myeloma plasma cells. They were tested for cytotoxicity in a 51Cr release assay. Pool-sensitized cells were capable of lysing autologous myeloma cells of type IgG Kappa (IgGK), but not of type IgG Lambda (IgG delta). Sensitization of lymphocytes to **allogeneic** myeloma cells of type

IgG delta led to lysis of both autologous and **allogeneic** myeloma cells of type IgG delta and IgGK, whereas sensitization to **allogeneic** IgGK myeloma cells failed to generate effector cells capable of lysing autologous or **allogeneic** myeloma cells. These results indicate that there exist distinct stimulating antigens and both distinct and common (cross-reacting) target antigens on human IgGK and IgG delta myeloma plasma cells.

L169 ANSWER 7 OF 21 CANCERLIT
ACCESSION NUMBER: 82090313 CANCERLIT
DOCUMENT NUMBER: 82090313
TITLE: Lymphocyte sensitization detected by the macrophage electrophoretic mobility assay in patients with renal cell carcinoma: Theophylline increases the sensitivity of the assay.
AUTHOR: Malkovsky M; Bubenik J; Malkovska V; Indrova M; Suhajova E; Jakoubkova J; Jira M
SOURCE: ARCHIV FUR GESCHWULSTFORSCHUNG, (1981). Vol. 51, No. 4, pp. 364-70.
Journal code: 746. ISSN: 0003-911X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 82090313
ENTRY MONTH: 198203
AB An antigen-induced release of a macrophage slowing factor (MSF) by peripheral blood lymphocytes was used to evaluate lymphocyte sensitization to various antigens in 30 patients with renal cell carcinoma (RCC) and in 14 normal individuals. Twenty-three of 30 (77%) patients with RCC, but no healthy controls were found to be sensitized to a soluble antigen prepared from an **allogeneic** kidney tumor by 3 M potassium chloride extraction. Peripheral blood lymphocytes from some patients with RCC displayed sensitization to protein isolated from fetal kidney (6 of 24; 25%), control "normal" kidney (6 of 30; 20%) and urinary bladder carcinoma (3 of 21; 14%) tissues. It has been suggested that cyclic adenosine 3' ,5'-monophosphate (cyclic AMP) could play a role in the mechanism of the MSF action (24). In agreement with this idea, the presence of 10-4 M theophylline enhanced the macrophage electrophoretic mobility (MEM) reduction caused by MSF. Furthermore, the DNA synthesis in lymphocytes (monitored by measuring the uptake of tritiated thymidine) on contact with phytohemagglutinin (PHA) was depressed in 9 of 21 (43%) patients with RCC as compared with healthy controls.

L169 ANSWER 8 OF 21 CANCERLIT
ACCESSION NUMBER: 81200447 CANCERLIT
DOCUMENT NUMBER: 81200447
TITLE: Immunotherapy versus chemotherapy of acute myeloid leukemia: response to PHA, **allogeneic** lymphocytes, and leukemic myeloblasts of remission lymphocytes from leukemia patients.
AUTHOR: Reizenstein P; Ogier C; Sjogren A M
SOURCE: RECENT RESULTS IN CANCER RESEARCH, (1980). Vol. 75, pp. 29-36.
Journal code: R1Y. ISSN: 0080-0015.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 81200447
ENTRY MONTH: 198108
AB Lymphocytes were studied from 51 patients with acute myeloid leukemia (AML) in remission given chemotherapy (CT) maintenance alone or given chemoimmunotherapy (CIT) with BCG and viable **allogeneic** leukemic cells. CT lymphocytes reacted significantly more to PHA (P less than 0.05)

if taken later than 100 days after remission than if taken earlier. CIT lymphocytes reacted less. Thus, the late CT lymphocytes reacted significantly more to nonspecific stimulators (PHA and **allogeneic** lymphocytes, P less than 0.01) than did late CIT lymphocytes or control lymphocytes. In consequence, the ratio of reactions to specific (leukemic myeloblasts) over nonspecific stimulators was significantly higher in CIT (P less than 0.01) than in CT lymphocytes. Results may indicate nonspecific immunostimulation during CT, and also some relative specific sensitization to **allogeneic** myeloblasts during CIT.

L169 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900478 CAPLUS
DOCUMENT NUMBER: 134:46754
TITLE: Use of semi-allogeneic cell line-peptide complexes for the treatment of cancer, AIDS and other viral diseases
INVENTOR(S): Gattoni-celli, Sebastiano; Shearer, Gene; Grene, Edith; Newton, Danforth A.; Brown, Edwin A.; Berzofsky, Jay A.; Degroot, Anne S.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secret, USA; Medical University of South Carolina
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076537	A2	20001221	WO 2000-US11008	20000424
WO 2000076537	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9811202	A1	19980319	WO 1997-US15920	19970910
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: WO 1997-US15920 A2 19970910
US 1999-254556 A2 19990616
US 1996-707920 A2 19960910

AB The present invention provides a compn. comprising a semi-allogeneic hybrid fusion cell and an immunogenic peptide. In particular, isolated peptides of HIV (Human Immunodeficiency Virus), HTLV-1, Hepatitis B virus, Hepatitis C virus, rubeola virus, influenza A virus and Human Papilloma Virus are provided in the compns. of the present invention. Moreover, isolated cancer-specific peptides specific to a cancer, for example, B cell lymphoma, T cell lymphoma, myeloma, leukemia, breast cancer, pancreatic cancer, colon cancer, lung cancer, renal cancer, liver cancer, prostate cancer, melanoma and cervical cancer are provided in the compns. of the present invention. Moreover, the present invention provides a

method of treating a subject infected by one or more of HIV, HTLV-1, Hepatitis B virus, Hepatitis C virus, rubeola virus, influenza A virus and Human Papilloma Virus, comprising administering a compn. comprising an effective amt. of a hybrid fusion cell and an effective amt. of an isolated immunogenic peptide of the virus in a pharmaceutically acceptable carrier. Further, the present invention provides a method of treating cancer in a subject with one or more of B cell lymphoma, T cell lymphoma, myeloma, leukemia, breast cancer, pancreatic cancer, colon cancer, lung cancer, renal cancer, liver cancer, prostate cancer, melanoma and cervical cancer, comprising administering a compn. comprising an effective amt. of a hybrid fusion cell and an effective amt. of an isolated immunogenic peptide of the cancer in a pharmaceutically acceptable carrier.

L169 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:859441 CAPLUS
DOCUMENT NUMBER: 134:130133
TITLE: Cross-priming of naive CD8 T cells against melanoma antigens using dendritic cells loaded with killed allogeneic melanoma cells
AUTHOR(S): Berard, Frederic; Blanco, Patrick; Davoust, Jean; Neidhart-Berard, Eve-Marie; Nouri-Shirazi, Mahyar; Taquet, Nicolas; Rimoldi, Donata; Cerottini, Jean Charles; Banchereau, Jacques; Palucka, A. Karolina
CORPORATE SOURCE: Baylor Institute for Immunology Research, Dallas, TX, 75204, USA
SOURCE: J. Exp. Med. (2000), 192(11), 1535-1543
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The goal of tumor immunotherapy is to elicit immune responses against autologous tumors. It would be highly desirable that such responses include multiple T cell clones against multiple **tumor antigens**. This could be obtained using the antigen presenting capacity of dendritic cells (DCs) and cross-priming. That is, one could load the DC with tumor lines of any human histocompatibility leukocyte antigen (HLA) type to elicit T cell responses against the autologous tumor. In this study, we show that human DCs derived from monocytes and loaded with killed melanoma cells prime naive CD45RA+CD27+CD8+ T cells against the four shared melanoma antigens: MAGE-3, gp100, tyrosinase, and MART-1. HLA-A201+ naive T cells primed by DCs loaded with HLA-A201- melanoma cells are able to kill several HLA-A201+ melanoma targets. Cytotoxic T lymphocyte priming towards melanoma antigens is also obtained with cells from metastatic melanoma patients. This demonstration of cross-priming against shared **tumor antigens** builds the basis for using allogeneic tumor cell lines to deliver **tumor antigens** to DCs for vaccination protocols.
REFERENCE COUNT: 38
REFERENCE(S): (1) Albert, M; Nat Med 1998, V4, P1321 CAPLUS
(2) Banchereau, J; Annu Rev Immunol 2000, V18, P767 CAPLUS
(3) Banchereau, J; Nature 1998, V392, P245 CAPLUS
(4) Boczkowski, D; J Exp Med 1996, V184, P465 CAPLUS
(5) Boon, T; Immunol Today 1997, V18, P267 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:613583 CAPLUS
DOCUMENT NUMBER: 131:227662
TITLE: Enhancement of immune response to **tumor antigens**
INVENTOR(S): Kaplan, Johanne; Gregory, Richard J.
PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946992	A1	19990923	WO 1999-US6039	19990319
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9931029	A1	19991011	AU 1999-31029	19990319
EP 1071333	A1	20010131	EP 1999-912716	19990319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-78889 P 19980320
WO 1999-US6039 W 19990319

AB This invention provides methods and compns. for breaking tolerance to a self-antigen, esp. in the context of a **tumor**-assocd. **antigen**. In one embodiment, dendritic cells are transduced to express **tumor antigens** derived from allogeneic or heterologous species to break immunol. tolerance and induce a cross-reactive immune response against the corresponding native or self-antigen.

REFERENCE COUNT: 8
REFERENCE(S):
(1) Bellone, M; Eur J Immunol 1991, V21, P2303 CAPLUS
(2) Chakraborty, M; J Immunotheraphy 1995, V18(2), P95 CAPLUS
(3) Infante, A; J Immunol 1991, V146(9), P2977 CAPLUS
(4) MacKay; US 5648219 A 1997 CAPLUS
(6) Pachner, A; Immunol Lett 1989, V20(3), P199 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:524124 CAPLUS
DOCUMENT NUMBER: 131:270914
TITLE: Anti-tumour activity against B16-F10 melanoma with a GM-CSF secreting allogeneic tumour cell vaccine
AUTHOR(S): Kayaga, J.; Souberbielle, BE; Sheikh, N.; Morrow, WJW; Scott-Taylor, T.; Vile, R.; Dalgleish, AG
CORPORATE SOURCE: Department of Oncology, St George's Hospital Medical School, London, SW17 ORE, UK
SOURCE: Gene Ther. (1999), 6(8), 1475-1481
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genetic modification of tumor cells with the GM-CSF encoding gene renders these cells more potent, as autologous tumor cell vaccine, than their wild-type counterparts. However, autologous vaccines are impractical for wide-scale clin. use and we have therefore investigated the efficacy of the GM-CSF genetic modification approach with an allogeneic whole cell tumor vaccine. In this report, we show that the allogeneic K1735-M2 (H-2k) melanoma cell vaccine induces a specific protective anti-tumor response against the syngeneic B16-F10 (H-2b) melanoma tumor in C57BL/6J mice. In vitro T cell work demonstrated that vaccination of animals with the allogeneic cell vaccine generated cytotoxic T cells specific for the autologous tumor. In vivo T cell subset depletion expts. also illustrated that this anti-tumor effect was mediated by both CD4+ve and CD8+ve T cells, suggesting that the allogeneic vaccine may operate through the "cross-priming" phenomenon whereby **tumor antigens** are

processed and presented to T cells by the host's own antigen presenting cells (APC). Thus, we transduced K1735-M2 cells with a GM-CSF expressing retroviral vector and showed anti-tumor activity of the GM-CSF secreting K1735-M2 cells as a therapeutic vaccine against the syngeneic B16-F10 tumor. Our data imply that GM-CSF genetically modified allogeneic whole cell tumor vaccines could be successful in the clinic. In addn., more potent combination gene therapy strategies could be tested using this therapeutic allogeneic vaccine model.

REFERENCE COUNT: 40
REFERENCE(S): (2) Aruga, A; Cancer Res 1997, V57, P3230 CAPLUS
(3) Ashley, D; J Neuroimmunol 1997, V78, P34 CAPLUS
(6) Bevan, M; J Exp Med 1995, V182, P639 CAPLUS
(8) Brichard, V; J Exp Med 1993, V178, P489 CAPLUS
(9) Castleden, S; Hum Gene Ther 1997, V8, P2087 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 13 OF 21 BIOSIS COPYRIGHT 2002 BIOSIS
ACCESSION NUMBER: 2001:151854 BIOSIS
DOCUMENT NUMBER: PREV200100151854
TITLE: Enhanced efficiency by centrifugal manipulation of adenovirus-mediated interleukin 12 gene transduction into human monocyte-derived dendritic cells.
AUTHOR(S): Nishimura, Naoki; Nishioka, Yasuhiko (1); Shinohara, Tsutomu; Sone, Saburo
CORPORATE SOURCE: (1) Third Department of Internal Medicine, School of Medicine, University of Tokushima, Kuramoto-cho 3, Tokushima, 770-8503: yasuhiko@clin.med.tokushima-u.ac.jp Japan
SOURCE: Human Gene Therapy, (March 1, 2001) Vol. 12, No. 4, pp. 333-346. print.
ISSN: 1043-0342.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Transduction of dendritic cells (DCs) with genes encoding **tumor-associated antigen** or with other genes that enhance immune reaction has been theorized to be potentially useful for enhancing the efficiency of DC-based **immunotherapy**. However, gene transduction of DCs generated from human peripheral blood monocytes has been of limited use because of the low efficiency. Here, we report that the efficiency of in vitro adenovirus-mediated gene transduction into human monocyte-derived DCs can be dramatically enhanced by centrifugation. The best conditions for centrifugal gene transduction were determined to be as follows: 2000 X g at 37degreeC for 2 hr at a multiplicity of infection (MOI) of 10 or greater. By this centrifugal method, approximately 88 and 70% of DCs were gene transducible at an MOI of 50 and 10, respectively. Functional analysis showed that DCs transduced with human interleukin 12 (IL-12)-expressing adenoviral vector under the optimal conditions of centrifugation stably produced IL-12 protein at high levels (8.1 ng/106 cells/48 hr). IL-12 gene-modified DCs (DC/IL-12) displayed a more mature phenotype than nontransduced DCs, as judged by decreased expression of CD1a and increased expression of CD83, B7.1 (CD80), B7.2 (CD86), and MHC class I and II molecules. DC/IL-12 showed a high phagocytic ability similar to nontransduced DCs and were significantly superior to control DCs in the **stimulation** of autologous and **allogeneic** T **lymphocyte** responses. The centrifugal transduction method with adenoviral vector might be useful for efficient generation of gene-modified DCs because it is very simple, highly efficient, reproducible, and not cytopathic. IL-12 gene-modified human DCs may be therapeutically useful as a good adjuvant in DC-based **immunotherapy**.

L169 ANSWER 14 OF 21 BIOSIS COPYRIGHT 2002 BIOSIS

ACCESSION NUMBER: 1993:300906 BIOSIS
DOCUMENT NUMBER: PREV199396019131
TITLE: Induction of cell-mediated immunity against B16-BL6 melanoma in mice **vaccinated** with cells modified by hydrostatic pressure and chemical crosslinking.
AUTHOR(S): Eisenthal, Avi; Ramakrishna, Venkatesh; Skornick, Yehuda; Shinitzky, Meir (1)
CORPORATE SOURCE: (1) Dep. Membrane Res. Biophysics, Weizmann Inst. Sci., P. O. Box 26, Rehovot 76100 Israel
SOURCE: Cancer Immunology Immunotherapy, (1993) Vol. 36, No. 5, pp. 300-306.
ISSN: 0340-7004.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In the preceding paper we have demonstrated an increase in presentation of both major histocompatibility complex antigens (MHC) and a **tumor -associated antigen** of the weakly immunogenic B16 melanoma by a straight-forward technique. The method consists in modulating the tumor cell membrane by hydrostatic pressure and simultaneous chemical crosslinking of the cell-surface proteins. In B16-BL6 melanoma, the induced antigenic modulation was found to persist for over 48 h, which permitted the evaluation of the ability of modified B16-BL6 cells to induce immunity against unomodified B16-BL6 cells. In the present study, we have shown that a significant systemic immunity was induced only in mice that were immunized with modified B16-BL6 melanoma cells, whereas immunization with unmodified B16-BL6 cells had only a marginal effect when compared to the results in control sham-immunized mice. The induced immunity was specific since a single immunization affected the growth of B16-BL6 tumors but had no efect on MCA 106, an antigenically unrelated tumor. The addition of interleukin-2 to the immunization regimen had no effect on the antitumor responses induced by a modified B16-BL6 cells. The cell-mediated immunity conferred by immunization with treated B16-BL6 cells was confirmed in experiments in vitro where splenocytes from immunized mice could be sensitized to proliferate by the presence of B16-BL6 cells. In addition, the altered antigenicity of these melanoma cells appeared to correlate with their increased susceptibility to specific effectors. Thus, 51Cr-labeled B16-BL6 target cells, modified by pressure and crosslinking, in comparison to control labeled target cells, were lysed in much greater number by effectors such as lymphokine-**activated** killer cells and **allogeneic** cytotoxic **lymphocytes** (anti-H-2-b), while such cells remained resistant to lysis by natural killer cells. Our findings indciate that the physical and chemical modifications of the tumor cells that are described here may be considered as a simple yet effective method for the preparation of tumor **vaccines**, which could be applied in tumor-bearing hosts.

L169 ANSWER 15 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999184590 EMBASE
TITLE: Dendritic cell-based vaccine: A promising approach for cancer immunotherapy.
AUTHOR: Tarte K.; Klein B.
CORPORATE SOURCE: B. Klein, INSERM U475, 99 rue Puech Villa, 39197 Montpellier Cedex 5, France
SOURCE: Leukemia, (1999) 13/5 (653-663).
Refs: 127
ISSN: 0887-6924 CODEN: LEUKED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
028 Urology and Nephrology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The unique ability of dendritic cells to pick up antigens and to activate naive and memory CD4+ and CD8+ T cells raised the possibility of using them to trigger a specific anti-tumor immunity. If numerous studies have shown a major interest in dendritic cell-based vaccines for cancer immunotherapy in animal models, only a few have been carried out in human cancers. In this review, we describe recent findings in the biology of dendritic cells that are important to generate anti-tumor cytotoxic T cells in vitro and we also detail clinical studies reporting the obtention of specific immunity to human cancers in vivo using reinfusion of dendritic cells pulsed with tumor antigens.

L169 ANSWER 16 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78209968 EMBASE
DOCUMENT NUMBER: 1978209968
TITLE: The modulation of tumour versus host response in lung, colon, and breast cancer patients: implications for adjuvant immunochemotherapy.
AUTHOR: Steward A.M.
CORPORATE SOURCE: Univ. Dept. Surg., St Vincent's Hosp., Melbourne, Australia
SOURCE: Australian and New Zealand Journal of Surgery, (1977) 47/5 (642-647).
CODEN: ANZJA7
COUNTRY: Australia
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
016 Cancer
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LANGUAGE: English
AB Major advances in the understanding of clinical tumour biology occurred with the appreciation that tumour-associated substances circulated in the blood of cancer patients. In this study their origin and immunogenic function have been investigated. Whole tumour cells (WTC) and cancer cell membrane fractions (CMF) of 24 patients with lung, colon, and breast cancer were investigated for their antigenic effect upon the patients' own lymphocytes and upon healthy **allogeneic** ones. The antigenicity of whole lung and breast cancer cells to **stimulate lymphocyte** DNA synthesis, and the ineffectiveness of colon cells were confirmed. CMF had little **stimulating** effect upon autologous **lymphocytes**; however, they were able to augment lymphocyte response to PPD and PHA in high dilution and to suppress it in high concentration. The serum of cancer patients exerted similar biphasic activity upon PPD and PHA **stimulated lymphocytes** ('lymphosuppressive-**stimulatory** factors, or LSSF). Sephadex studies confirmed that LSSF activity in cancer serum correlated with circulating CMF. These substances modulate lymphocyte nucleic acid synthesis in vitro; it is likely that they similarly modulate the patient tumour-host cell relationship.

L169 ANSWER 17 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76096063 EMBASE
DOCUMENT NUMBER: 1976096063
TITLE: Effect of bacillus Calmette Guerin immunotherapy on tumor antigen induced **lymphocyte stimulated** protein synthesis in melanoma patients.
AUTHOR: Roth J.A.; Golub S.H.; Holmes E.C.; Morton D.L.
CORPORATE SOURCE: Surg. Serv., VA Hosp., Sepulveda, Calif., United States
SOURCE: Surgery, (1975) 78/1 (66-75).
CODEN: SURGAZ
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
016 Cancer
026 Immunology, Serology and Transplantation
013 Dermatology and Venereology
009 Surgery
006 Internal Medicine
LANGUAGE: English
AB Changes in in vitro **lymphocyte stimulation** protein synthesis (SPS) of 40 melanoma patients following incubation with 3M KCl extracts of **allogenic** melanoma, lung carcinoma, and sarcoma antigens and phytohemagglutinin (PHA) were quantitated by measuring H3 leucine uptake. One of eleven 'untreated' melanoma patients stimulated significantly to the melanoma antigen. However, this lymphocyte response was not significantly different from that of the normal subjects. Patients who received systemic bacillus Calmette Guerin (BCG) by the tine technique for 3 mth and for 6 mth had significant increase in lymphocyte protein synthesis following incubation with melanoma antigen. There were no significant differences in PHA responses between the 'untreated' melanoma patients and the BCG treated group. Testing of serial lymphocyte samples from nine melanoma patients before treatment and at monthly intervals thereafter confirmed these observations. Furthermore, no change in serial complement fixing antibody titers to melanoma antigen was noted in the BCG treated patients. These results demonstrated that in vitro lymphocyte responses to melanoma antigen may be augmented by BCG therapy.

L169 ANSWER 18 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 74025147 EMBASE
DOCUMENT NUMBER: 1974025147
TITLE: In vitro studies of cellular mediated immunostimulation of tumor growth.
AUTHOR: Fidler I.J.
CORPORATE SOURCE: Dept. Pathol., Sch. Dent. Med., Univ. Pennsylvania, Philadelphia, Pa. 19174, United States
SOURCE: Journal of the National Cancer Institute, (1973) 50/5 (1307-1312).
CODEN: JNCIAM
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
013 Dermatology and Venereology
030 Pharmacology
LANGUAGE: English
AB The interaction of normal, sensitized, and concanavalin A (Con A) **stimulated** isogeneic, **allogeneic**, and/or xenogeneic **lymphocytes** with the B16 melanoma, C57BL/6J and/or A/J mouse embryo cells was examined by an in vitro colony inhibition **stimulation** test. Various numbers of **lymphocytes** were mixed with target cells, incubated for 2 hours in a rotating test tube, and then plated in culture dishes. Three and 7 days later, dishes were fixed and stained, and target cells were counted. Specifically and non specifically sensitized lymphocytes, at ratios up to 1000:1, repeatedly and significantly enhanced target cell growth. At higher lymphocyte doses, colony inhibition was evident. The importance of the relative plating efficiency of target systems in the interpretation of results of in vitro cytotoxicity tests is discussed. Rat Con A **stimulated** **lymphocytes** also enhanced tumor growth, whereas dead lymphocytes or supernatants derived from cultures containing Con A **stimulated** **lymphocytes** did not. Sensitized **lymphocytes** appeared to enhance tumor growth by direct interaction. These results support the hypothesis and experimental data by Prehn that the immune response may have a dual role in its relationship to the development of neoplasms.

L169 ANSWER 19 OF 21 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-365402 [31] WPIDS
DOC. NO. NON-CPI: N2000-273460
DOC. NO. CPI: C2000-110300
TITLE: Universal **tumor-associated antigens** such as telomerase catalytic subunit capable of binding major histocompatibility complex molecule useful for diagnosis, prevention and treatment of cancer.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HAHN, W C; NADLER, L M; SCHULTZE, J L; VONDERHEIDE, R H
PATENT ASSIGNEE(S): (DAND) DANA FARBER CANCER INST INC; (WHED) WHITEHEAD INST BIOMEDICAL RES
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000025813	A1	20000511	(200031)*	EN	130
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP US					
AU 2000013311	A	20000522	(200040)		
EP 1126872	A1	20010829	(200150)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000025813	A1	WO 1999-US25438	19991029
AU 2000013311	A	AU 2000-13311	19991029
EP 1126872	A1	EP 1999-956777	19991029
		WO 1999-US25438	19991029

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000013311	A	Based on	WO 200025813
EP 1126872	A1	Based on	WO 200025813

PRIORITY APPLN. INFO: US 1998-106106P 19981029
AB WO 200025813 A UPAB: 20000630
NOVELTY - A universal **tumor-associated antigen** (TAA), or a peptide, that binds to a major histocompatibility complex molecule (MHC), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an ex vivo generated cytotoxic T lymphocyte (I) that kills a cell expressing human telomerase catalytic subunit (hTERT) or TAA, in a hTERT or TAA specific MHC-restricted fashion;

(2) an ex vivo generated antigen presenting cell (II) that presents a peptide of TAA, or hTERT;

(3) a hTERT peptide which bind to a MHC molecule;

(4) treating a patient comprising or is at a risk of comprising a cell expressing TAA by administering a nucleic acid molecule (III) encoding TAA, where the peptide expressed by the nucleic acid is processed by an antigen presenting cell which activates cytotoxic T lymphocytes and kills cells expressing TAA;

(5) identifying TAA, comprising:

(a) analyzing one or more databases, to identify a gene expressed in more than one or at least one human tumor type, at a level 3-fold higher than the level expressed in a normal human cell;

(b) using a computer-run algorithm to identify an amino acid sequence in the protein encoded by the gene that is predicted to bind to MHC;

(c) synthesizing an immunogen that comprises the amino acid sequence identified in (b), or a sequence that is predicted by a computer-run algorithm to bind MHC with higher affinity than the sequence; and

(d) testing the ability of the immunogen to stimulate a MHC restricted cytotoxic T lymphocyte response that is specific for the protein; and

(6) a method of assessing immunity levels, to TAA, in a patient, comprising measuring the level of cytotoxic T lymphocytes specific for the antigen, in a patient sample.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine; activator of cytotoxic T lymphocytes (CTL). CD3+CD8+CTLs specific for hTERT peptide (ILAKFLHWL) obtained from peripheral blood mononuclear cells (PBMC) were tested for their ability to kill tumor cells in an hTERT-dependent manner. Dendritic cells prepared from PBMC were pulsed with 40 mu g/ml of the peptide, beta 2-microglobulin (3 mu g/ml) for 4 hours at 37 deg. C and added to autologous CD8-enriched T cells in a media containing 10% human serum, glutamine and interleukin (IL)-7. After 7 days T cell cultures were harvested and restimulated with peptide-pulsed autologous CD40-activated B cells followed by adding IL2. The results showed that CTLs generated by stimulation with hTERT peptide lysed hTERT-positive cells.

USE - TAA, (I), (II) or a peptide that binds to class I major histocompatibility complex (MHC), is useful for treating a patient at a risk of comprising a tumor cell expressing TAA, especially human telomerase catalytic subunit (hTERT), where TAA or the peptide is processed by antigen presenting cell and activates an autologous or **allogenic** cytotoxic T **lymphocyte** to kill the cell that expresses TAA in an antigen-specific, MHC-restricted fashion. The class I MHC molecule is preferably an HLA-A2 or HLA-A3 molecule. Measuring the level of (I) in a sample is useful for assessing the level of immunity of a patient to a TAA or a peptide, where the sample is obtained before or after a cancer treatment is given to the patient. All claimed. TAA peptides (e.g. hTERT) are also useful for diagnosis and prophylactic treatment of cancer.

Dwg.0/9

L169 ANSWER 20 OF 21 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-561740 [47] WPIDS
DOC. NO. CPI: C1999-163700
TITLE: Freezing dendritic cells, useful for presenting antigen and educating immune effector cells.
DERWENT CLASS: B04 D16
INVENTOR(S): NICOLETTE, C A; SHANKARA, S
PATENT ASSIGNEE(S): (GENZ) GENZYME CORP
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9946984	A1	19990923	(199947)*	EN	73
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP US					
AU 9931025	A	19991011	(200008)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9946984	A1	WO 1999-US6033	19990319
AU 9931025	A	AU 1999-31025	19990319

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9931025	A	Based on	WO 9946984

PRIORITY APPLN. INFO: US 1998-78929P 19980320

AB WO 9946984 A UPAB: 19991116

NOVELTY - A method (I) for freezing dendritic cells (DCs) is new and comprises suspending the DCs in media comprising at least 30% human-derived serum and reducing the temperature of the suspension to below -80 deg. C, therefore freezing dendritic cells.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a substantially purified population of DCs produced by (I); and

(2) a method for ex vivo generation of antigen-specific immune effector cells, comprising educating immune effector cells by co-culture with the DCs.

USE - Substantially purified population of dendritic cells (DCs) frozen and thawed are useful for presenting antigen and for educating immune effector cells which are administered to a subject in an effective amount to induce an immune response specific to the antigen presented by the DC. The agents are administered to subjects or individuals susceptible to at risk of developing disease, e.g. cancer.

ADVANTAGE - The method is useful for producing a substantial portion of the DCs frozen with retained viability and functionality when thawed. The DCs are also substantially purified.

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L169 ANSWER 21 OF 21 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-251050 [22] WPIDS
DOC. NO. CPI: C1998-078247
TITLE: New immunogenic compositions for tumour therapy - comprising stimulated **lymphocytes** **allogenic** to a human patient and **tumour** **-associated antigen** obtained from the patient.
DERWENT CLASS: B04 D16
INVENTOR(S): GRANGER, G A; HISERODT, J C; THOMPSON, J A
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9816238	A2	19980423	(199822)*	EN	72
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9748242	A	19980511	(199837)		
NO 9901691	A	19990609	(199933)		
EP 930887	A2	19990728	(199934)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1237909	A	19991208	(200016)		
BR 9712988	A	20001024	(200058)		
MX 9903341	A1	19990901	(200067)		
KR 2000049096	A	20000725	(200116)		
US 6207147	B1	20010327	(200119)		
JP 2001509135	W	20010710	(200144)		102

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9816238	A2		WO 1997-US18718	19971010
AU 9748242	A		AU 1997-48242	19971010
NO 9901691	A		WO 1997-US18718	19971010
			NO 1999-1691	19990409
EP 930887	A2		EP 1997-910999	19971010
			WO 1997-US18718	19971010
CN 1237909	A		CN 1997-199908	19971010
BR 9712988	A		BR 1997-12988	19971010
			WO 1997-US18718	19971010
MX 9903341	A1		MX 1999-3341	19990409
KR 2000049096	A		WO 1997-US18718	19971010
			KR 1999-703176	19990412
US 6207147	B1	Provisional	US 1996-28548P	19961011
			US 1997-948939	19971010
JP 2001509135	W		WO 1997-US18718	19971010
			JP 1998-517803	19971010

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9748242	A	Based on	WO 9816238
EP 930887	A2	Based on	WO 9816238
BR 9712988	A	Based on	WO 9816238
KR 2000049096	A	Based on	WO 9816238
JP 2001509135	W	Based on	WO 9816238

PRIORITY APPLN. INFO: US 1996-28548P 19961011; US 1997-948939 19971010

AB WO 9816238 A UPAB: 19980604

An immunogenic composition (A) suitable for administration to a human, comprises a combination of: (a) stimulated **lymphocytes allogenic** to the human; and (b) **tumour-associated antigen** (TAA) from the human.

Also claimed are: (1) an immunogenic composition suitable for administration to a human, comprising a combination of: (a) **lymphocytes allogenic** to the human; (b) leukocytes **allogenic** to the **lymphocytes**; and (c) an inactivated tumour cell population, consisting of primary tumour cells obtained from the human, or the progeny of such cells; (2) a method for stimulating an anti-tumour immunological response in a human, comprising: (a) mixing ex vivo a first cell population comprising tumour cells, and a second cell population comprising **lymphocytes allogenic** to the patient, to produce a cell mixture; and (b) administering an immunogenic amount of the cell mixture to the human; (3) a method for treating a neoplastic disease in a human, comprising: (a) mixing ex vivo a first cell population comprising tumour cells, and a second cell population comprising **lymphocytes allogenic** to the patient, to produce a cell mixture; and (b) administering the cell mixture to the human; and (4) a cell population for simultaneous, separate or sequential use in a method of treatment of a human by surgery or therapy, or for eliciting an anti-tumour immunological response in the human patient, containing: (a) **alloactivating lymphocytes allogenic** to a human patient; and (b) primary tumour cells from the human patient or progeny.

USE - The compositions of (A) and (1) can be used to provide potent immunostimulation for an anti tumor response (claimed) or to elicit a response against simultaneously injected TAA. As a result, a cellular immune response emerges that is specific for the tumour, and much stronger

than can be achieved by simply administering the patient's tumour cells, or a derivative. The compositions can be administered to patients either to treat or palliate a clinically detectable tumour, or for prophylaxis, particularly after surgical debulking, chemotherapy or radiation therapy of a previously detectable tumour. The compositions are typically administered at a location distant from the original tumour, for stimulating a systemic reactivity against the primary tumour and metastases. The reactivity may in turn eradicate or slow the development of tumour cells, either at the primary site, within metastases (if there are any) or both. A kit comprising separate containers can be used to produce a composition as in (A) or (1), the kits keep the components separate and the cells in 1(a) are obtained by coculture of **lymphocytes allogenic** to the human and leukocytes **allogenic** to the **lymphocytes** (claimed). The cells as in (4) can be used to manufacture a medicament that is antitumor or ellicts an antitumor response (claimed).
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